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RAPPORT

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SYSTEMATIC LITERATURE SEARCH WITH A SORTED REFERENCE LIST

Laboratory diagnosis of tick-borne infections

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Key message

The Norwegian Directorate of Health and The Norwegian National Advisory Unit on Tick-borne diseases asked The Norwegian Institute of Public Health to perform a systematic literature search followed by an overview of available research on laboratory diagnosis and co-infections of tick-borne diseases. We performed the work in two parts.

Objective
The objective of **part one** was to identify research on laboratory diagnosis of people with long-term complaints after borrelia infection, including seven tick-born infections other than Lyme borreliosis (Borrelia) and tick-borne encephalitis (TBE): anaplasmosis (Anaplasma phagocytophilium), rickettsiosis (Rickettsia helvetica or Rickettsia conorii), neoehrlichiosis (Candidatus Neoehrlichia mikurensis), babesiois (Babesia spp, hard tick-borne relapsing fever (Borrelia miyamotoi), tularemia (Francisella tularensis) and cat scratch disease (Bartonella spp). The objective of **part two** was to identify research on tick-borne co-infections, also including Lyme borreliosis (Borrelia) and tick-borne encephalitis (TBE).

Method
We performed a systematic literature search for research published between 2007 and 2018, and categorized potentially relevant references according to the studied infections and study design.

Results
Part 1: Laboratory diagnostics:
We included and sorted 458 references by type of tick-borne infection and by study design (diagnostic studies, case studies or case series).

Part 2: Co-infections: We found four systematic reviews, eleven non-systematic reviews, 15 diagnostic studies, 50 prevalence studies and 25 case-studies on Lyme borreliosis co-infections.

We did not read the papers in full text, and we did not assess the methodological quality of the studies, nor did we summarize the results. We present references to the studies with links to the studies' abstracts or fulltext.

Hovedfunn

Folkehelseinstituttet fikk i oppdrag av Helsedirektoratet og Flåttsenteret (Nasjonal kompetansetjeneste for flåttbårne sykdommer) å foreta et systematisk litteratursøk for å kartlegge eksisterende forskning på laboratoriediagnostikk av flåttbårne sykdommer. Vi utførte oppdraget i to deler.

Formål
Formålet med **del 1** var å identifisere forskning på metoder for laboratoriediagnostikk av personer med langvarige plager etter borreliainfeksjon, inkludert syv andre flåttbårne sykdommer enn borreliose og skogflåttencefalitt (TBE): anaplasmose (Anaplasma phagocytophilium), rickettsioser (Rickettsia Helvetica eller Rickettsia Conorii), neoehrlichiose (Candidatus Neoehrlichia mikurensis), babesiose (Babesia spp), tilbakefallsfeber (Borrelia miyamotoi), harepest (Francisella tularensis) og katteklorfeber (Bartonella spp). Formålet med **del 2** var å identifisere forskning på koinfeksjoner ved flåttbitt, også inkludert borrelia og skogflåttencefalitt (TBE).

Metode
Vi utførte et systematisk søk etter forskning publisert mellom 2007 og 2018 og sorterte mulig relevante referanser etter infeksjonstype og studiedesign.

Resultat

Del 1: Laboratoriediagnostikk
Vi inkluderte og sorterte 458 referanser etter flåttbårne infeksjonstyper og studiedesign (diagnostiske studier, kasuistikker og case serier).

Del 2: Koinfeksjoner
Vi fant fire systematiske oversikter, elleve ikke-systematiske oversiktsartikler, 15 diagnosestudier, 50 forekomststudier og 25 kasusistikker på borrelia koinfeksjoner.

Vi har ikke lest studiene i full tekst, vurdert studienes metodiske kvalitet eller oppsummert resultater. Vi presenterer referanser til studiene med lenker til studienes sammendrag eller fulltekst.

Contents

Preface

The Norwegian Directorate of Health has initiated a Nordic collaboration regarding diagnosis and follow up of patients with long-term complaints suspected to be associated with tick-borne diseases. The aim is to establish a Nordic consensus for medical assessment and follow-up of patients with suspected tick-borne infections. The Norwegian Institute of Public Health, Division of Infection Control and Environmental Health is a member of the Nordic consensus working group, and is responsible for Workpackage 1: Systematic literature search on diagnostics of tick-borne infections.

We have performed a systematic literature search to identify possibly relevant research on the diagnosis of patients with long-term complaints after suspected tick-borne diseases.
The project group consisted of the following members, all from The Norwegian Institute of Public Health:

- Ingvild Kirkehei (project leader), research librarian,
  Cluster for Reviews and Health Technology Assessments
- Signe Flottorp, research director,
  Cluster for Reviews and Health Technology Assessments
- Audun Aase, department director,
  Department for Infectious Disease Immunology
- Ingeborg Aaberge, specialist director
  Division of Infection Control and Environmental Health

We thank the Nordic consensus group lead by The Norwegian National Advisory Unit on Tick-borne diseases for input, and Elisabet Hafstad for peer review of the search strategy.

Hege Kornør	Kåre Birger Hagen	Ingvild Kirkehei
Department director	*Research director*	*Project leader*

Background

The incidence of tick-borne infections is increasing in the Nordic countries, and so is the awareness and fear of tick bites and tick-borne infections in the public. The healthcare system has access to guidelines and recommendations for the diagnosis of the most common tick-borne diseases, Lyme borreliosis (caused by the bacterium Borrelia burgdorferi) and tick-borne encephalitis (TBE, caused by the tick-borne encephalitis virus (TBEV), a member of the family Flaviviridae) (1-6). Newer recommendations for patients with long-term complaints after borrelia infection, sometimes referred to as *chronic Lyme disease* or *Lyme disease with persistent symptoms,* are scarce*.* There are also few recommendations for the diagnosis of other, less prevalent tick-borne infections.

Other relevant tick-borne infections in the Nordic countries are (7-9):

- anaplasmosis (caused by the bacterium Anaplasma phagocytophilium*)*
- rickettsioses (caused by the bacteria Rickettsia helvetica and Rickettsia conorii)
- neoehrlichiosis (caused by the bacterium Candidatus Neoehrlichia mikurensis)
- babesiois (caused by the parasite Babesia spp.)
- hard tick relapsing fever (caused by the bacterium Borrelia miyamotoi)
- tularemia (caused by the bacterium Francisella tularensis)
- cat scratch disease (caused by the bacterium Bartonella spp.)

Some people may be infected with more than one of these pathogens at the same time. Such co-infections may lead to more severe symptoms and make the diagnosis more complex (10).

Objective

The aim of this report is to provide an overview of published research from 2007 to 2018 on:

1. the performance of laboratory tests for the diagnosis of tick-borne diseases other than Lyme borreliosis and TBE.
2. the prevalence and laboratory diagnosis of patients with tick-borne co-infections.

This may include studies that aim to answer the following clinical questions:

- In patients with long-term complaints possibly related to previous tick bite(s) and with negative laboratory diagnostic tests for borrelia infection, what other diagnostic tests could be performed to diagnose or exclude other tick-borne infections?
- Which methods for laboratory diagnosis of other tick-borne infections than borreliosis and TBE are relevant in patients after tick bite(s)?
- In patients with long-term complaints after borrelia infection, what other diagnostic tests could be performed to investigate if the patient also have a tick-borne infection other than borreliosis?
- Are there any laboratory tests that can reliably support the diagnosis of persisting borrelia infection in spite of antibiotic treatment?

Systematic literature review with a sorted reference list

This kind of research overview may be referred to as a systematic literature search with a sorted reference list. In a systematic literature search with a sorted reference list, we perform a systematic literature search based on one or more clinical questions. The search is comprehensive and rigorously developed to find all potentially relevant articles. The search strategy must be documented and verifiable (11). We screen the references from the search to sift out the non-relevant references, and we then present the possibly relevant references in lists or tables. We do not retrieve the fulltexts, we do not perform any critical appraisal of the studies and we do not report or summarize the studies' results.

Included study types

In this report, we have included references to research with different study designs.

Systematic review: "A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review."(12)

Diagnostic study: Diagnostic research can be categorized into four phases, with studies answering four different types of questions (13):

1. Do test results in affected patients differ from those in normal individuals?
2. Are patients with certain test results more likely to have the target disorder?
3. Do test results distinguish patients with and without the target disorder among those in whom it is clinically sensible to suspect the disorder?
4. Do patients undergoing the diagnostic test fare better than similar untested patients?

The three first diagnostic questions can be examined with studies with cross sectional, case control or cohort designs. The last question is a question about the clinical effectiveness of a diagnostic test, hence best evaluated in a randomized trial.

Case studies and case series: Descriptive studies reporting on something that has happened or been observed with a single patient (case study) or a set of patients (case series). The studies mainly focus on the manifestations, clinical course, and prognosis or outcome for the patient (14).

Prevalence study: "A type of cross-sectional study that measures the prevalence of a characteristic". Prevalence is "the proportion of a population having a particular condition or characteristic"(12).

Methods

We divided the work into two parts:

- Part 1: Laboratory diagnoses of tick-borne infections
- Part 2: Co-infections of tick-borne infections

In both parts, we performed a systematic literature search, and screened through the search results according to predefined selection criteria.

Selection criteria

Part 1 – Laboratory diagnoses of tick-borne infections

Population:	Adults, young people and children with long-term complaints after tick bite ("chronic Lyme disease" or "post treatment Lyme syndrome") or with symptoms of the following infections: - anaplasmosis *(*Anaplasma phagocytophilium) - rickettsiosis (Rickettsia helvetica or Rickettsia conorii) - neoehrlichiosis (Candidatus Neoehrlichia mikurensis) - babesiois (Babesia sp.) - hard tick relapsing fever (Borrelia miyamotoi) - tularemia (Francisella tularensis) - cat scratch disease (Bartonella spp.)
Diagnostic methods:	All laboratory methods identified in the literature search were relevant, e.g. enzyme-linked immunosorbent assays (ELISA), immunofluorescent assays (IFA), immunoblotting, polymerase chain reaction (PCR), microscopy and culture.
Comparison:	For diagnostic studies: Reference test. All methods were relevant for inclusion.
Outcomes:	Statistical measures of diagnostic performance or test accuracy measures, such as sensitivity/specificity, positive predictive value, negative predictive value, likelihood ratios.

	We did not exclude studies based on reported outcomes.
Study design:	Systematic reviews, cross sectional studies, case control studies. We also included case series and case studies mentioning diagnoses or diagnostic tests in the abstract.
Publication year:	Laboratory methods used before 2007 are less relevant today, and thus we limited the search to publication years 2007-2018.
Language:	All languages
Exclusion:	Because of already existing guidelines, we excluded studies on tests for the diagnosis of tick-borne encephalitis (TBE) and early localized- and disseminated Lyme borreliosis. We excluded studies on infections in ticks and domestic or wild animals.

Part 2 – Co-infections

Inclusion:	All studies reporting prevalence or diagnostic methods for identifying co-infections between two or more of the ten infections included in part 1 about diagnostic tests. In addition, we included studies on all stages of Lyme borreliosis and tick-borne encephalitis (TBE). This search was also limited to publication year 2007-2018.
Exclusion:	We excluded studies on patients with other co-infections than tick-borne diseases, e.g. HIV.

Literature search

A research librarian (Kirkehei) performed systematic searches based on the inclusion criteria.

Part 1 – Laboratory diagnoses of tick-borne infections

We searched the following databases: MEDLINE (Ovid), Embase (Ovid), Cochrane Database of Systematic Reviews (Cochrane Library), Database of Abstracts of Reviews of Effects (CRD DARE), Health Technology Assessments Database (CRD HTA), Epistemonikos, ISI Web of Science, Scopus, Prospero, Clinical Trials.gov, WHO International Clinical Trials Registry Platform (ICTRP).

All searches are reported in detalis in Appendix 1. Another librarian, the project group and the Nordic expert group on systematic review of scientific literature on diagnostic methods for tick-borne diseases assured the quality of the search strategies.

Kirkehei performed the searches in January 2018. The searches consisted of subject headings and freetext terms describing the included tick-borne diseases and terms typically used when describing diagnostics (for instance diagnosis, sensitivity, specificity) or relevant study designs (for instance cross-sectional studies). The first search was limited to studies mentioning "ticks" (and other terms describing tick-bites) in the title or abstract. In a second supplementary search, we removed this limitation.
The search was limited to publication year as of 2007. We excluded studies on animals or ticks (without mentioning humans) from the search.

Part 2 – Co-infections

We searched the following databases: MEDLINE (Ovid), Embase (Ovid), Epistemonikos, ISI Web of Science.

Kirkehei performed the searches in August 2018. The search consisted of subject headings and freetext terms describing the included tick-borne diseases, limited to terms describing "co-infections" (e.g. co-occuring infections, simultaneous infections). The search was limited to publication year as of 2007. There were no limits to study design. We excluded studies on animals or ticks (without mentioning humans) from the search.

Selection and sorting of relevant studies

References from the literature search were exported to the online screening tool Covidence. Two people independently screened all references (Kirkehei, Flottorp, Aaberge or Aase), and we resolved disagreements through discussion. We screened the references based on title and abstract, and we did not read the studies in full text.

Included references were exported to the reference managent system EndNote, where one person (Kirkehei) sorted the references into categories by infection type, study design (diagnostic studies or case studies/case series) and publication year. The project group checked the final sorting result.

Initially, we planned to categorize references according to type of diagnostic study, e.g. case control og cross sectional studies assessing if the test can be used to sort sick from healthy people (diagnostic phase 1 studies) and cross sectional studies comparing the diagnostic test to be assessed with a reference test (diagnostic phase 3 studies). However, we found it difficult to do this based on abstracts only, and decided to present all diagnostic studies in one category.

In part 1 (diagnostic tests) we also extracted information on diagnostic methods studied or used. Kirkehei extracted information about the tests used based on the information provided in the abstracts and the project group helped standardize the text.

We categorized and extracted data based on the titles and abstracts only and this may have led us to include irrelevant references. To ascertain relevance and to assess methodolocical quality it is necessary to read the studies in full text.

Due to copyright restrictions, we have not included abstracts in the report. The reader may follow the internet link to the publication's abstract and possibly available full text.

Results part 1: Laboratory diagnosis of tick-borne infections

The search resulted in 3916 unique references, wheras we included and sorted 458 references according to infection type.

In Table 1 we have summarized the numbers of included and sorted references.

Table 1 Summary of number of references included

	Systematic reviews	Diagnostic studies	Case studies or case series
Different infections		6	3
Longterm complaints after tick-bites ("Chronic Lyme disease»)	1	4	11
Aanaplasmosis *(*Anaplasma phagocytophilium)		4	44
Rickettsiosis (Rickettsia helvetica, Rickettsia Conorii)		8	49
Neoehrlichiosis (Candidatus Neoehrlichia mikurensis)			5
Babesiois (Babesia sp.)	1	27	86
Hard tick relapsing fever (Borrelia miyamotoi)		4	11
Tularemia (Francisella tularensis)		23	21
Cat scratch disease (Bartonella spp)	1	24	125

In the following chapters, we present tables with the included references and information about the diagnostic tests used. We use the following abbreviations:

- PCR: polymerase chain reaction
- IFA: immune fluorescent assay
- WB: Western blot
- ELISA: Enzymelinked immunosorbent assay

1 Diagnosis of more than one infection

Some references referred to studies on diagnosis of more than one of the mentioned tick-borne diseases, and we present them in a separate category (six diagnostic studies and three case studies/case series). Studies on co-infections are presented in another chapter, page 83.

1.1 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Schlachter S, Chan K, Marras SAE, Parveen N. **Detection and Differentiation of Lyme Spirochetes and Other Tick-Borne Pathogens from Blood Using Real-Time PCR with Molecular Beacons**. Methods in Molecular Biology 2017;1616:155-170. https://link.springer.com/protocol/10.1007%2F978-1-4939-7037-7_10	Real time PCR
2.	**Development of a Pathogen Blood Test for patients with Lyme-like symptoms.** ACTRN12615000202561. Australian New Zealand Clinical Trials Registry, 2015. https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=367991	PCR
3.	Chan K, Marras SA, Parveen N. **Sensitive multiplex PCR assay to differentiate Lyme spirochetes and emerging pathogens Anaplasma phagocytophilum and Babesia microti**. BMC Microbiology 2013;13:295. https://bmcmicrobiol.biomedcentral.com/articles/10.1186/1471-2180-13-295	Multiplex PCR
4.	Source TP, Group PS. **300 Antibody Diagnostic Test Kit**. NCT01646411. ClinicalTrials.gov, 2012. https://clinicaltrials.gov/ct2/show/NCT01646411	300 Antibody Diagnostic Test Kit
5.	Karan LS, Koliasnikova NM, Toporkova MG, Makhneva MA, Nadezhdina MV, Esaulkova AI, et al. [**Usage of real time polymerase chain reaction for diagnostics of different tick-borne infections.] [Russian**] Zhurnal mikrobiologii, epidemiologii, i immunobiologii 2010 (3):72-77. https://www.ncbi.nlm.nih.gov/pubmed/20734723	Real time PCR vs serological data
6.	Angelakis E, Roux V, Raoult D, Rolain JM. **Real-time PCR strategy and detection of bacterial agents of lymphadenitis**. European Journal of Clinical Microbiology & Infectious Diseases 2009;28(11):1363-1368. https://link.springer.com/article/10.1007%2Fs10096-009-0793-6	Real time PCR vs standard 16 S rRNA gene amplification and sequencing.

1.2 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Galloo X, Wiels W, Du Four S, Surmont M, Mertens R. **Beyond lyme: Tick-borne illness in Europe.** Acta Clinica Belgica: International Journal of Clinical and Laboratory Medicine 2016;71 (Supplement 1):40. https://www.tandfonline.com/doi/pdf/10.1080/17843286.2016.1250435?needAccess=true	Not reported in abstract/abstract not available
2.	Greenberg R. **Tick-borne infections and pediatric bipolar disorder**. Bipolar Disorders 2015;(1):62-3. https://onlinelibrary.wiley.com/doi/pdf/10.1111/bdi.12309	Lyme: ELISA and WB IgG/IgM Babesia and Bartonella: IgG/IgM titers and fluo-rescent insitu hybridization (FISH) tests Other pathogens: IgG/IgM titers.
3.	Shchuchinova LD. [**Serological verification of tick-borne encephalitis cases in the Altai Republic**.] [Article in Russian] Meditsinskaia Parazitologiia i Parazitarnye Bolezni 2014;(2):10-3. https://www.ncbi.nlm.nih.gov/pubmed/25296419	Serology

2 Longterm complaints after tick bite (chronic Lyme disease)

We found one systematic review, three diagnostic studies and ten case studies or case series on the diagnosis of "chronic Lyme disease".

2.1 Systematic reviews

	Reference	Diagnostic test(s) studied
1.	Borgermans L, Goderis G, Vandevoorde J, Devroey D. **Relevance of chronic lyme disease to family medicine as a complex multidimensional chronic disease construct: a systematic review**. International Journal of Family Medicine Print 2014;2014:138016. https://www.hindawi.com/journals/ijfm/2014/138016/	Different tests studied

2.2 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Fallon BA, Pavlicova M, Coffino SW, Brenner C. **A Comparison of Lyme disease serologic test results from 4 laboratories in patients with persistent symptoms after antibiotic treatment**. Clinical Infectious Diseases 2014;59(12):1705-1710. https://academic.oup.com/cid/article/59/12/1705/2895616	IgM and IgG WBs, C6 ELISA, Whole cell sonicate ELISA
2.	Schwarzbach A. **Diagnostic novelties of chronic lyme/neuroborreliosis**. Journal of Gastrointestinal and Liver Diseases 2012;(4):22. http://www.jgld.ro/2012/supplement4/supplement4.pdf	IB , ELISA and a multianalyte technique

3.	Aalto A, Sjowall J, Davidsson L, Forsberg P, Smedby O. **Brain magnetic resonance imaging does not contribute to the diagnosis of chronic neuroborreliosis**. Acta Radiologica 2007;48(7):755-762. http://journals.sagepub.com/doi/abs/10.1080/02841850701367903?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed&	Brain magnetic resonance imaging (MRI)

2.3 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Florens N, Lemoine S, Guebre-Egziabher F, Valour F, Kanitakis J, Rabeyrin M, et al. **Chronic Lyme borreliosis associated with minimal change glomerular disease: a case report**. BMC Nephrology 2017;18(1):51. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5292808/	ELISA IGM og IgG
2.	Haney C, Nahata MC. **Unique expression of chronic Lyme disease and Jarisch-Herxheimer reaction to doxycycline therapy in a young adult**. BMJ Case Reports 2016;2016:009433. https://casereports.bmj.com/content/2016/bcr-2013-009433.long	Not reported in abstract/abstract not available
3.	Garakani A, Mitton AG. **New-onset panic, depression with suicidal thoughts, and somatic symptoms in a patient with a history of lyme disease**. Case Reports Psychiatry 2015;2015:457947. https://www.hindawi.com/journals/crips/2015/457947/	Not reported in abstract/abstract not available
4.	Matera G, Labate A, Quirino A, Lamberti AG, Borz AG, Barreca GS, et al. **Chronic neuroborreliosis by B. garinii: an unusual case presenting with epilepsy and multifocal brain MRI lesions**. New Microbiologica 2014;37(3):393-397. http://www.newmicrobiologica.org/PUB/allegati_pdf/2014/3/393.pdf	Not reported in abstract/abstract not available
5.	Palmieri JR, King S, Case M, Santo A. **Lyme disease: case report of persistent Lyme disease from Pulaski County, Virginia**. International Medical Case Reports Journal 2013;6:99-105. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3862396/	ELISA, IgM og IgG Western blot
6.	Kowacs PA, Martins RT, Piovesan EJ, Pinto MC, Yoshinari NH. **Chronic unremitting headache associated with Lyme disease-like illness**. Arquivos de Neuro-Psiquiatria 2013;71(7):470-473. https://www.ncbi.nlm.nih.gov/pubmed/23857618	Not reported in abstract/abstract not available

7.	Baranova NS, Spirin NN, Nizovtzeva LA, Pakhomova YA, Fadeeva OA. **Clinical and instrumental characteristics of chronic neuroborreliosis**. Zhurnal Nevrologii I Psikhiatrii Imeni S S Korsakova 2012;112(9):40-47. https://www.ncbi.nlm.nih.gov/pubmed/23235423	Not reported in abstract/abstract not available
8.	Markeljevic J, Sarac H, Rados M. **Tremor, seizures and psychosis as presenting symptoms in a patient with chronic lyme neuroborreliosis (LNB)**. Collegium Antropologicum 2011;35 Suppl 1:313-318. https://www.ncbi.nlm.nih.gov/pubmed/21648354	Serum and CSF serology as well as EEG and EMNG evaluation
9.	Wagner V, Zima E, Geller L, Merkely B. **Acute atrioventricular block in chronic Lyme disease. Hungarian**. Orvosi Hetilap 2010;151(39):1585-1590. https://akademiai.com/doi/abs/10.1556/OH.2010.28965	Not reported in abstract/abstract not available
10.	Gavino AC, Andea A, Hughey L, Magro C, Balmer N. **Superantigen ID reaction secondary to chronic lyme disease**. American Journal of Dermatopathology 2010;32(4):406. https://journals.lww.com/amjdermatopathology/Citation/2010/06000/Abstracts_Presented_at_the_13th_Joint_Meeting_of.19.aspx	WB

3 Anaplasmosis (Anaplasma phagocytophilum)

We found four diagnostic studies and 44 case studies/case series on anaplasmosis (anaplasma phagocytophilum).

3.1 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Chung IH, Austin AL, Massung RF, Kato CY. **Clinical validation of new and existing anaplasma phagocytophilum real-time PCR assays**. American Journal of Tropical Medicine and Hygiene 2014;(1):33. https://www.ajtmh.org/content/journals/10.4269/ajtmh.2014.91.5_Suppl_1.astmh_14_abstracts_1_250	Real-time PCR assays

2.	Schotthoefer AM, Meece JK, Ivacic LC, Bertz PD, Zhang K, Weiler T, et al. **Comparison of a real-time PCR method with serology and blood smear analysis for diagnosis of human anaplasmosis: importance of infection time course for optimal test utilization**. Journal of Clinical Microbiology 2013;51(7):2147-2153. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3697711/	PCR and serology
3.	Pan L, Zhang L, Wang G, Liu Q, Yu Y, Wang S, et al. **Rapid, simple, and sensitive detection of Anaplasma phagocytophilum by loop-mediated isothermal amplification of the msp2 gene**. Journal of Clinical Microbiology 2011;49(12):4117-4120. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3232955/	PCR
4.	Al-Khedery B, Barbet AF. **Comparative genomics identifies a potential marker of human-virulent Anaplasma phagocytophilum**. Pathogens 2014;3(1):25-35. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4235736/	Simple PCR test

3.2 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Sigurjonsdottir VK, Feder HM, Wormser GP. **Anaplasmosis in pediatric patients: Case report and review**. Diagnostic Microbiology and Infectious Disease 2017;89(3):230-4. https://www.sciencedirect.com/science/article/pii/S0732889317302444?via%3Dihub	Not reported in abstract/abstract not available
2.	Marko D, Perry AM, Ponnampalam A, Nasr MR. **Cytopenias and clonal expansion of gamma/delta T-cells in a patient with anaplasmosis: a potential diagnostic pitfall**. Journal of Clinical & Experimental Hematopathology 2017;56(3):160-4. https://www.jstage.jst.go.jp/article/jslrt/56/3/56_160/_article	Peripheral blood smear, bone marrow evaluation, serology
3.	Lee SH, Park SY, Jang MJ, Choi KJ, Lee HK, Cho YU, et al. **Clinical Isolation of Anaplasma phagocytophilum in South Korea**. American Journal of Tropical Medicine & Hygiene 2017;97(6):1686-90. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5805025/	Microscopic examination and serology

4.	Lagler H, Harrison N, Kussmann M, Obermuller M, Burgmann H, Makristathis A, et al. **Direct detection of Anaplasma phagocytophilum by polymerase chain reaction followed by electrospray ionization mass spectrometry from human blood**. International Journal of Infectious Diseases 2017;60:61-3. https://linkinghub.elsevier.com/retrieve/pii/S1201-9712(17)30142-X	Commercial system based on PCR followed by electrospray ionization mass spectrometry (ESI-MS).
5.	Kim CM, Kim SW, Kim DM, Yoon NR, Jha P, Jang SJ, et al. **Case report: Polymerase chain reaction testing of tick bite site samples for the diagnosis of Human Granulocytic Anaplasmosis**. American Journal of Tropical Medicine & Hygiene 2017;97(2):403-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5544070/	PCR with buffy coat and crust samples
6.	Mujahid R, Colon-Cartagena W. **A heart-breaking tick bite. Case of a patient with Human Granulocytic Anaplasmosis Cardiomyopathy**. Journal of the American Geriatrics Society 2016;(1):S93. https://onlinelibrary.wiley.com/doi/abs/10.1111/jgs.14231	PCR
7.	Fine AB, Sweeney JD, Nixon CP, Knoll BM. **Transfusion-transmitted anaplasmosis from a leukoreduced platelet pool**. Transfusion 2016;56(3):699-704. https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.13392	PCR and ELISA
8.	Welc-Faleciak R, Kowalec M, Zajkowska J, Pancewicz SA, Sinski E. **Clinical and molecular features of one case of human infection with Anaplasma phagocytophilum from Podlaskie Province in eastern Poland**. Annals of Agricultural & Environmental Medicine 2015;22(3):414-7. http://www.aaem.pl/Clinical-and-molecular-features-of-one-case-of-human-infection-with-Anaplasma-phagocytophilum,72300,0,2.html	PCR
9.	Cooper JD, Dometita D, Hasan A, Dorion P, Wolk DM, Martinez RM. **"Orange" You Glad You Checked the Buffy Coat?** Clinical Microbiology Newsletter 2015;37(2):9-13. https://www.sciencedirect.com/science/article/pii/S0196439915000021	Acridine orange buffy coat fluorescent stain
10.	von Wissmann B, Hautmann W, Sing A, Hizo-Teufel C, Fingerle V. **Assessing the risk of human granulocytic anaplasmosis and lyme borreliosis after a tick bite in Bavaria, Germany**. Ijmm International Journal of Medical Microbiology 2015;305(7):736-41. https://linkinghub.elsevier.com/retrieve/pii/S1438-4221(15)00089-2	Serology

11.	Solar VR, Mendoza De La Garza M, Treadwell T. **Heart failure and atrial fibrillation triggered by anaplasmosis in an elderly female**. Journal of the American Geriatrics Society 2015;(1):S244. https://onlinelibrary.wiley.com/doi/10.1111/jgs.13439	peripheral smear, PCR
12.	Shields K, Cumming M, Rios J, Wong MT, Zwicker JI, Stramer SL, et al. **Transfusion-associated Anaplasma phagocytophilum infection in a pregnant patient with thalassemia trait: a case report**. Transfusion 2015;55(4):719-25. https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.12908	Not reported in abstract/abstract not available
13.	Lee S, Khankhanian P, Salama C, Brown M, Lieber J. **Pseudo-Pelger-Huet anomaly and granulocytic dysplasia associated with human granulocytic anaplasmosis**. International Journal of Hematology 2015;102(1):129-33. https://link.springer.com/article/10.1007%2Fs12185-015-1769-1	Peripheral blood smear
14.	Kaphle U, Kheir F, Thammasitboon S. **A Rare Case of ARDS From Human Anaplasmosis**. Respiratory Care 2015;60(7):e125-7. http://rc.rcjournal.com/content/60/7/e125.short	Not reported in abstract/abstract not available
15.	Selvaraj V, Leyse J, Magauran C. **Deceptively simple or simply deceptive!** Journal of the American Geriatrics Society 2014;(1):S289. https://onlinelibrary.wiley.com/doi/abs/10.1111/jgs.12870	PCR
16.	Rand JV, Tarasen AJ, Kumar J, Homan SM, Tobin E. **Intracytoplasmic granulocytic morulae counts on confirmed cases of ehrlichiosis/anaplasmosis in the Northeast**. American Journal of Clinical Pathology 2014;141(5):683-6. https://academic.oup.com/ajcp/article/141/5/683/1761257	Peripheral smears
17.	Kim KH, Yi J, Oh WS, Kim NH, Choi SJ, Choe PG, et al. **Human granulocytic anaplasmosis, South Korea, 2013**. Emerging Infectious Diseases 2014;20(10):1708-11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4193166/	Seroconversion, PCR, and sequence analysis
18.	Hing M, Woestyn S, van Bosterhaut B, Desbonnet Y, Heyman P, Cochez C, et al. **Diagnosis of human granulocytic anaplasmosis in Belgium by combining molecular and serological methods**. New Microbes and New Infections 2014;2(6):177-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4265051/	Not reported in abstract/abstract not available
19.	Ohashi N, Gaowa, Wuritu, Kawamori F, Wu D, Yoshikawa Y, et al. **Human granulocytic Anaplasmosis, Japan**. Emerging Infectious Diseases 2013;19(2):289-92.	Serology

	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3559047/	
20.	Rand JV, Tarasen A, Homan S, Kumar J, Tobin E. **Intracytoplasmic granulocytic morulae counts on confirmed cases of human granulocytic ehrlichiosis/anaplasmosis in the northeastern united states**. Laboratory Investigation 2013;(1):374A. https://academic.oup.com/ajcp/article/141/5/683/1761257	Peripheral smears
21.	Koff G, Sellers J, Oxman D. **Anaplasmosis and ARDS**. Critical Care Medicine 2013;(1):A316. https://journals.lww.com/ccmjournal/Abstract/2013/12001/1231__Anaplasmosis_and_ARDS.1181.aspx	Serology, PCR
22.	Bautista MT, Sharma R, Orenstein A, Circeo L. **Myocardial dysfunction and shock from human granulocytic anaplasmosis (HGA): An unusual presentation**. Critical Care Medicine 2013;(1):A295-A6. https://journals.lww.com/ccmjournal/Abstract/2013/12001/1164__Myocardial_dysfunction_and_Shock_from_Human.1116.aspx	PCR
23.	Alhumaidan H, Westley B, Esteva C, Berardi V, Young C, Sweeney J. **Transfusion-transmitted anaplasmosis from leukoreduced red blood cells**. Transfusion 2013;53(1):181-6. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1537-2995.2012.03685.x	Peripheral blood smear, serology and PCR
24.	Weil AA, Baron EL, Brown CM, Drapkin MS. **Clinical findings and diagnosis in human granulocytic anaplasmosis: A case series from Massachusetts**. Mayo Clinic Proceedings 2012;87(3):233-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3498394/	PCR
25.	Koebel C, Kern A, Edouard S, Hoang AT, Celestin N, Hansmann Y, et al. **Human granulocytic anaplasmosis in eastern France: clinical presentation and laboratory diagnosis**. Diagnostic Microbiology & Infectious Disease 2012;72(3):214-8. https://linkinghub.elsevier.com/retrieve/pii/S0732-8893(11)00516-5	PCR and serology
26.	Jereb M, Pecaver B, Tomazic J, Muzlovic I, Avsic-Zupanc T, Premru-Srsen T, et al. **Severe human granulocytic anaplasmosis transmitted by blood transfusion**. Emerging Infectious Diseases 2012;18(8):1354-7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3414041/	Not reported in abstract/abstract not available
27.	Edouard S, Koebel C, Goehringer F, Socolovschi C, Jaulhac B, Raoult D, et al. **Emergence of human granulocytic anaplasmosis in France**. Ticks & tick-borne Diseases 2012;3(5-6):403-5.	Serology and molecular biology

	https://www.sciencedirect.com/science/article/pii/S1877959X12000866?via%3Dihub	
28.	Annen K, Friedman K, Eshoa C, Horowitz M, Gottschall J, Straus T. **Two cases of transfusion-transmitted Anaplasma phagocytophilum**. American Journal of Clinical Pathology 2012;137(4):562-5. https://academic.oup.com/ajcp/article/137/4/562/1760673	Not reported in abstract/abstract not available
29.	Weil A, Baron E, Brown C, Drapkin M. **Detection of Anaplasma phagocytophilum infections: A case series from a Suburban Community Hospital in Massachusetts**. American Journal of Tropical Medicine and Hygiene 2011;(1):82. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2923137/	rtPCR assays followed by nested PCR and sequence analysis
30.	Qasba N, Feder HM, Campbell WA, Egan JF, Shamshirsaz AA. **A case report of human granulocytic anaplasmosis (Ehrlichiosis) in pregnancy and a literature review of tick-borne diseases in the united states during pregnancy**. Obstetrical and Gynecological Survey 2011;66(12):788-96. https://www.ncbi.nlm.nih.gov/pubmed/22192463	Not reported in abstract/abstract not available
31.	Liu QH. **Pay attention to differential diagnosis of anaplasmosis with thrombocytopenic syndrome**. International Journal of Infectious Diseases 2011;1):S112. https://www.ijidonline.com/article/S1201-9712(11)60391-3/abstract	Serology and PCR
32.	Kanjilal S, Brutsaert E, Markoff B. **Anaplasmosis: A case report and literature review**. Journal of Hospital Medicine 2011;(2):S197. https://www.shmabstracts.com/abstract/anaplasmosis-a-case-report-and-literature-review/	Peripheral blood smear, confirmed with buffy coat and serologies
33.	Ghera P, Kasirye Y, Choudhry MW, Shaw GR, Ejercito VS. **Acute transient sensorineural hearing loss due to Anaplasma phagocytophilum**. Wmj 2011;110(6):288-90. http://www.wisconsinmedicalsociety.org/_WMS/publications/wmj/pdf/110/6/288.pdf	Giemsa-stained peripheral blood smear and PCR
34.	Novakova M, Vichova B, Majlathova V, Lesnakova A, Pochybova M, Pet'ko B. **First Case of Human Granulocytic Anaplasmosis from Slovakia**. Annals of Agricultural and Environmental Medicine 2010;17(1):173-5. https://www.ncbi.nlm.nih.gov/pubmed/20684497	PCR
35.	Haschke-Becher E, Bernauer R, Walleczek AM, Apfalter P, Afazel-Saeedi S, Kraus J, et al. **First detection of the Anaplasma phagocytophilum groEL-A genotype in man**. Journal of Infection 2010;60(4):300-5.	PCR

	https://linkinghub.elsevier.com/retrieve/pii/S0163-4453(09)00394-6	
36.	Santos AS, de Sousa R, Alves F, Proenca P, Nuncio MS, Dumler JS, et al. **Isolation of Coxiella burnetii from the blood of a patient with positive Anaplasma phagocytophilum serological results**. Clinical Microbiology & Infection 2009;15 Suppl 2:192-3. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(14)63541-2/fulltext	Not reported in abstract/abstract not available
37.	Hulinska D, Votypka J, Vanousova D, Hercogova J, Hulinsky V, Drevova H, et al. **Identification of Anaplasma phagocytophilum and Borrelia burgdorferi sensu lato in patients with erythema migrans**. Folia Microbiologica 2009;54(3):246-56. https://link.springer.com/article/10.1007%2Fs12223-009-0039-0	PCR, blood smears, cultivation, IFA
38.	Schneider JG. **Human ehrlichiosis: a case study**. Clinical Laboratory Science 2009;22(1):3-8. https://www.ncbi.nlm.nih.gov/pubmed/19354021	Not reported in abstract/abstract not available
39.	Hindryckx P, D'Heygere F. **A 42-year-old man with persistent fever after holiday. Dutch**. Tijdschrift voor Geneeskunde 2009;65(11):495-6.	Serology
40.	Psaroulaki A, Koliou M, Chochlakis D, Ioannou I, Mazeri S, Tselentis Y. **Anaplasma phagocytophilum infection in a child**. Pediatric Infectious Disease Journal 2008;27(7):664-6. https://insights.ovid.com/pubmed?pmid=18536621	PCR
41.	Centers for Disease C, Prevention. **Anaplasma phagocytophilum transmitted through blood transfusion--Minnesota, 2007**. MMWR - Morbidity & Mortality Weekly Report 2008;57(42):1145-8. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5742a1.htm	PCR
42.	Young NP, Klein CJ. **Encephalopathy with seizures having PCR-positive Anaplasma phagocytophilum and Ehrlichia chaffeensis**. European Journal of Neurology 2007;14(2):e3-4. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1468-1331.2006.01582.x	Not reported in abstract/abstract not available
43.	Peris-Garcia J, Cuadrado-Pastor JM, Jover-Diaz F, Botas-Velasco M. **Probable case of imported human anaplasmosis**. Enfermedades Infecciosas y Microbiologia Clinica 2007;25(10):656-7. https://www.ncbi.nlm.nih.gov/pubmed/18053479	Not reported in abstract/abstract not available

44.	Dhand A, Nadelman RB, Aguero-Rosenfeld M, Haddad FA, Stokes DP, Horowitz HW. **Human granulocytic anaplasmosis during pregnancy: case series and literature review**. Clinical Infectious Diseases 2007;45(5):589-93. https://academic.oup.com/cid/article/45/5/589/274600	Not reported in abstract/abstract not available

4 Rickettsiosis (Rickettsia conorii or R helvetica)

We found eight diagnostic studies and 49 case studies/case series on rickettsia conoriii or helvetica.

4.1 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Khrouf F, Sellami H, Elleuch E, Hattab Z, Ammari L, Khalfaoui M, et al. **Molecular diagnosis of Rickettsia infection in patients from Tunisia**. Ticks & tick-borne Diseases 2016;7(5):653-656. https://linkinghub.elsevier.com/retrieve/pii/S1877-959X(16)30024-3	Quantitative real time PCR vs. reverse line blot test
2.	Znazen A, Sellami H, Elleuch E, Hattab Z, Ben Sassi L, Khrouf F, et al. **Comparison of two quantitative real time PCR assays for Rickettsia detection in patients from Tunisia**. PLoS Neglected Tropical Diseases [electronic resource] 2015;9(2):e0003487. http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003487	rtPCRs
3.	Bizzini A, Peter O, Baud D, Edouard S, Meylan P, Greub G. **Evaluation of a new serological test for the detection of anti-Coxiella and anti-Rickettsia antibodies**. Microbes & Infection 2015;17(11-12):811-816. https://www.sciencedirect.com/science/article/pii/S1286457915001999?via%3Dihub	IFA
4.	Renvoise A, Rolain JM, Socolovschi C, Raoult D. **Widespread use of real-time PCR for rickettsial diagnosis**. FEMS Immunology & Medical Microbiology 2012;64(1):126-129. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1574-695X.2011.00899.x	rt PCR

5.	Mouffok N, Socolovschi C, Raoult D. **Eschar swabbing for diagnosis of mediterranean spotted fever (Rickettsia conorii)**. Tropical Medicine and International Health 2011;(1):269. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3310672/	rtPCR
6.	Kantso B, Svendsen CB, Jorgensen CS, Krogfelt KA. **Evaluation of serological tests for the diagnosis of rickettsiosis in Denmark**. Journal of Microbiological Methods 2009;76(3):285-288. https://www.sciencedirect.com/science/article/pii/S0167701208004351?via%3Dihub	-IFA, Weil-Felix test
7.	Do EJ, Kim JE, Park JM, Lee KM, Jung MY, Lee HJ, et al. **Development of recombinant OmpA and OmpB proteins as diagnostic antigens for rickettsial disease**. Microbiology & Immunology 2009;53(7):368-374. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1348-0421.2009.00142.x	ELISA
8.	Boretti FS, Perreten A, Meli ML, Cattori V, Willi B, Wengi N, et al. **Molecular Investigations of Rickettsia helvetica infection in dogs, foxes, humans, and Ixodes ticks**. Appl Environ Microbiol 2009;75(10):3230-3237. http://aem.asm.org/content/75/10/3230.full	PCR

4.2 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Luke N, Munasinghe H, Balasooriya L, Premaratna R. **Widespread subcutaneous necrosis in spotted fever group Rickettsioses from the coastal belt of Sri Lanka- a case report**. BMC Infectious Diseases 2017;17(1):278. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-017-2375-z	Not reported in abstract/abstract not available
2.	Colomba C, Trizzino M, Giammanco A, Bonura C, Di Bona D, Tolomeo M, et al. **Israeli Spotted Fever in Sicily. Description of two cases and minireview**. International Journal of Infectious Diseases 2017;61:7-12. https://www.sciencedirect.com/science/article/pii/S1201971217301145?via%3Dihub	Not reported in abstract/abstract not available

3.	Tzanetakos D, Papadopoulou M, Kanellopoulos D, Mamali M, Safarikas M, Katsianos D, et al. **Chronic inflammatory demyelinating polyneuropathy associated with Rickettsia conorii: First case report**. Journal of the Neurological Sciences 2016;371:60-1. https://www.jns-journal.com/article/S0022-510X(16)30646-3/abstract	Routine serological testing and brain/cervical MRI
4.	Mansueto P, Seidita A, Bongiovi A, Catalano T, Pirrone G, Cusimano C, et al. **Multiple organ failure as onset of mediterranean spotted fever: A review based on a case**. Italian Journal of Medicine 2016;10(3):195-201. https://www.italjmed.org/index.php/ijm/article/view/itjm.2016.625	Not reported in abstract/abstract not available
5.	Kostopoulou V, Chochlakis D, Kanta C, Katsanou A, Rossiou K, Rammos A, et al. **A Case of Human Infection by Rickettsia slovaca in Greece**. Japanese Journal of Infectious Diseases 2016;69(4):335-7. https://www.jstage.jst.go.jp/article/yoken/69/4/69_JJID.2015.194/_article	Not reported in abstract/abstract not available
6.	Hsairi M, Ben Ameur S, Alibi S, Belfitouri Y, Maaloul I, Znazen A, et al. **Macrophagic activation syndrome related to an infection by Rickettsia conorii in a child**. Archives de Pediatrie 2016;23(10):1076-9. https://www.sciencedirect.com/science/article/pii/S0929693X16303293?via%3Dihub	Serology
7.	Colomba C, Siracusa L, Trizzino M, Gioe C, Giammanco A, Cascio A. **Myocarditis in mediterranean spotted fever: A case report and a review of the literature**. JMM Case Reports 2016;3(4). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5330236/	Not reported in abstract/abstract not available
8.	Chochlakis D, Bongiorni C, Partalis N, Tselentis Y, Psaroulaki A. **Possible Rickettsia massiliae Infection in Greece: an Imported Case**. Japanese Journal of Infectious Diseases 2016;69(4):328-30. https://www.jstage.jst.go.jp/article/yoken/69/4/69_JJID.2015.195/_article	Not reported in abstract/abstract not available
9.	Caisso C, Payan J, Dunais B, Neri D, Vassallo M. **A case of uveitis due to Rickettsia conorii infection in Southeastern France**. Ticks and Tick-borne Diseases 2016;7(2):338-41. https://www.sciencedirect.com/science/article/pii/S1877959X15300455?via%3Dihub	IFA
10.	Santos-Antunes J, Nunes ACR, Macedo G. **Mediterranean spotted fever in a patient with Crohn's disease under adalimumab: First case report and review of the literature**. Gastroenterologia y Hepatologia 2015;38(6):379-87. http://www.elsevier.es/es-revista-gastroenterologia-hepatologia-14-articulo-mediterranean-spotted-fever-in-patient-S0210570514001812	Not reported in abstract/abstract not available

11.	Nogueras MM, Roson B, Lario S, Sanfeliu I, Pons I, Anton E, et al. **Coinfection with "Rickettsia sibirica subsp. mongolotimonae" and Rickettsia conorii in a Human Patient: a Challenge for Molecular Diagnosis Tools**. Journal of Clinical Microbiology 2015;53(9):3057-62. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4540899/	Not reported in abstract/abstract not available
12.	Dzelalija B, Punda-Polic V, Medic A, Mraovic B, Simurina T. **A case of Mediterranean spotted fever associated with severe respiratory distress syndrome**. Microbes & Infection 2015;17(11-12):870-3. https://www.sciencedirect.com/science/article/pii/S1286457915001781?via%3Dihub	IFA
13.	Dikme O, Topacoglu H. **Mediterranean spotted fever in the emergency department. Turkish**. Akademik Acil Tip Olgu Sunumlari Dergisi 2015;6(4):69-71. https://www.researchgate.net/publication/281498940_Mediterranean_Spotted_Fever_in_the_Emergency_Department	Not reported in abstract/abstract not available
14.	Del Prete E, Pizzanelli C, Moretti P, Cosottini M, Bonuccelli U. **Mediterranean spotted fever: an unusual clinical and neuroradiological presentation**. Neurological Sciences 2015;36(11):2141-3. https://www.ncbi.nlm.nih.gov/pubmed/26152799	Not reported in abstract/abstract not available
15.	Barja Lopez JM, Bahamonde Carrasco A, Alija Senra A, Manjon Haces JA, Soto del Moral F. **Mediterranean spotted fever with lymphangitis occurring from a tick bite lesion. A case in Spain**. International Journal of Dermatology 2015;54(10):e430-1. https://onlinelibrary.wiley.com/doi/full/10.1111/ijd.12885	Not reported in abstract/abstract not available
16.	Abroug N, Khairallah-Ksiaa I, Kahloun R, Khochtali S, Zaouali S, Khairallah M. **Parinaud's oculoglandular syndrome revealing subclinical Rickettsia conorii infection**. International Ophthalmology 2015;35(5):717-9. https://link.springer.com/article/10.1007%2Fs10792-015-0094-2	IFA
17.	Zijlstra M, Heidema J, Lukkassen I. **A boy with an eschar and a rash**. Nederlands Tijdschrift voor Geneeskunde 2014;158:A7238. https://www.ntvg.nl/artikelen/een-jongen-met-een-eschar-en-huiduitslag	Serology
18.	Salva I, de Sousa R, Gouveia C. **Rickettsial meningitis**. BMJ Case Reports 2014;10:10. https://casereports.bmj.com/content/2014/bcr-2013-203283	Serology
19.	Meslin P, Renoux MC, Manin C, Wendremaire P, Rosselini D, Tambat A, et al. **A 2-month-old baby with Mediterranean spotted fever. French**. Archives de Pediatrie 2014;21(7):772-5.	Serology and PCR

	https://www.sciencedirect.com/science/article/pii/S0929693X14001778?via%3Dihub	
20.	Mandelcwajg A, Menager C, Cheron G. **Mediterranean spotted fever in a 3-year-old child**. Archives de Pediatrie 2014;21(4):396-8. https://www.sciencedirect.com/science/article/pii/S0929693X14000311?via%3Dihub	Not reported in abstract/abstract not available
21.	Kozhevnikova GM, Tokmalaev AK, Voznesensky SL, Karan LS. **South African tick bite fever in a group of Russian tourists**. Terapevticheskii Arkhiv 2014;86(11):82-3. https://www.ncbi.nlm.nih.gov/pubmed/25715493	IFA
22.	Hanen L, Mouna S, Faten F, Raida BS, Moez J, Yosra C, et al. **An unusual cause of optic neuritis: Rickettsiosis disease**. Asian Pacific Journal of Tropical Biomedicine 2014;4(12):998-1000. https://www.sciencedirect.com/science/article/pii/S2221169115301180	Serology
23.	Fernandez-Flores A, De Cabo-Lopez E, Diaz-Galvez FJ. **Cutaneous findings in a case of Mediterranean spotless fever due to Rickettsia conorii, with gangrene of multiple toes**. American Journal of Dermatopathology 2014;36(2):e22-5. https://insights.ovid.com/pubmed?pmid=23719481	Not reported in abstract/abstract not available
24.	Colomba C, Imburgia C, Trizzino M, Titone L. **First case of Mediterranean spotted fever-associated rhabdomyolysis leading to fatal acute renal failure and encephalitis**. International Journal of Infectious Diseases 2014;26:12-3. https://www.sciencedirect.com/science/article/pii/S1201971214014325?via%3Dihub	Not reported in abstract/abstract not available
25.	Ben Mansour N, Barakett N, Hajlaoui N, Haggui A, Filali T, Dahmen R, et al. **Acute myocarditis complicating Mediterranean spotted fever. A case report**. Annales de Cardiologie et d'Angeiologie 2014;63(1):55-7. https://www.sciencedirect.com/science/article/pii/S0003392811000801?via%3Dihub	Serology
26.	Lecronier M, Prendki V, Gerin M, Schneerson M, Renvoise A, Larroche C, et al. **Q fever and Mediterranean spotted fever associated with hemophagocytic syndrome: case study and literature review**. International Journal of Infectious Diseases 2013;17(8):e629-33. https://www.sciencedirect.com/science/article/pii/S1201971213000398?via%3Dihub	Not reported in abstract/abstract not available
27.	Gehrke FS, Angerami RN, Marrelli MT, de Souza ER, do Nascimento EM, Colombo S, et al. **Molecular characterization of mediterranean spotted fever rickettsia isolated from a European traveler in the state of Sao Paulo, Brazil**. Journal of Travel Medicine 2013;20(1):54-6.	PCR

	https://academic.oup.com/jtm/article/20/1/54/1817319	
28.	Kularatne SA, Weerakoon KG, Rajapakse RP, Madagedara SC, Nanayakkara D, Premaratna R. **A case series of spotted fever rickettsiosis with neurological manifestations in Sri Lanka**. International Journal of Infectious Diseases 2012;16(7):e514-7. https://www.sciencedirect.com/science/article/pii/S1201971212000938?via%3Dihub	IFA
29.	Joshi HS, Thomas M, Warrier A, Kumar S. **Gangrene in cases of spotted fever: A report of three cases**. BMJ Case Reports 2012;1448. https://casereports.bmj.com/content/2012/bcr-2012-007295.long	Not reported in abstract/abstract not available
30.	Duque V, Ventura C, Seixas D, Barai A, Mendonca N, Martins J, et al. **Mediterranean spotted fever and encephalitis: A case report and review of the literature**. Journal of Infection and Chemotherapy 2012;18(1):105-8. https://www.sciencedirect.com/science/article/pii/S1341321X12703574	Not reported in abstract/abstract not available
31.	Rombola F. **Mediterranean spotted fever presenting as an acute pancreatitis**. Acta Gastroenterologica Belgica 2011;74(1):91-2. https://www.ncbi.nlm.nih.gov/pubmed/21563660	Not reported in abstract/abstract not available
32.	Ozturk Engin D, Kuloglu F, Sengoz Inan A, Ceran N, Cakar S, Goktas P. **Mediterranean spotted fever: Report of two cases**. Turkiye Klinikleri Journal of Medical Sciences 2011;31(6):1554-8. http://www.turkiyeklinikleri.com/article/en-mediterranean-spotted-fever-report-of-two-cases-61379.html	IFA, PCR
33.	Dissanayake NLA, Madegedara D. **An unusual case of fatal pulmonary hemorrhage in pregnancy**. Lung India 2011;28(3):205-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3162761/	Not reported in abstract/abstract not available
34.	Agahan ALD, Torres J, Fuentes-Paez G, Martinez-Osorio H, Orduna A, Calonge M. **Intraocular inflammation as the main manifestation of Rickettsia conorii infection**. Clinical Ophthalmology 2011;5(1):1401-7.	Serology according to the European Guidelines
35.	Yilmaz E, Akalin H, Mistik R, Heper Y, Engin A, Kilicaslan E, et al. **Mediterranean spotted fever: Retrospective evaluation of 16 cases. Turkish**. Trakya Universitesi Tip Fakultesi Dergisi 2010;27(2):167-71. https://www.researchgate.net/publication/263673206_Mediterranean_Spotted_Fever_Retrospective_Evaluation_Of_16_Cases	IFA

36.	Nilsson K, Elfving K, Pahlson C. **Rickettsia helvetica in patient with meningitis, Sweden, 2006**. Emerging Infectious Diseases 2010;16(3):490-2.	PCR
37.	Figueira-Coelho J, Martins T, Machado J, Maltez F. **Atypical case of Mediterranean spotted fever**. Brazilian Journal of Infectious Diseases 2010;14(3):213-6. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-86702010000300001	Not reported in abstract/abstract not available
38.	de Almeida DN, Favacho AR, Rozental T, Barcaui H, Guterres A, Gomes R, et al. **Fatal spotted fever group rickettsiosis due to Rickettsia conorii conorii mimicking a hemorrhagic viral fever in a South African traveler in Brazil**. Ticks & tick-borne Diseases 2010;1(3):149-50. https://www.sciencedirect.com/science/article/pii/S1877959X1000049X?via%3Dihub	Molecular and immunohistochemical analyses
39.	Romdhane FB, Loussaief C, Toumi A, Yahia SB, Khaiyrallah M, Bouzouaia N, et al. **Mediterranean spotted fever: A report of 200 cases in Tunisia**. Clinical Microbiology and Infection 2009;15(SUPPL. 2):209-10. https://www.ncbi.nlm.nih.gov/pubmed/19456798	Not reported in abstract/abstract not available
40.	Premaratna R, Chandrasena TG, Rajapakse RP, Eremeeva ME, Dasch GA, Bandara NK, et al. **Rickettsioses presenting as major joint arthritis and erythema nodosum: description of four patients**. Clinical Rheumatology 2009;28(7):867-8. https://link.springer.com/article/10.1007%2Fs10067-009-1166-3	Serology
41.	Pinna A. **Ocular manifestations of rickettsiosis: 1. Mediterranean spotted fever: laboratory analysis and case reports**. International Journal of Medical Sciences 2009;6(3):126-7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2659483/	Not reported in abstract/abstract not available
42.	Nilsson K. **Septicaemia with Rickettsia helvetica in a patient with acute febrile illness, rash and myasthenia**. Journal of Infection 2009;58(1):79-82. https://www.ncbi.nlm.nih.gov/pubmed/18649945	PCR together with serology
43.	Laurent M, Voet A, Libeer C, Lambrechts M, Van Wijngaerden E. **Mediterranean spotted fever, a diagnostic challenge in travellers**. Acta Clinica Belgica 2009;64(6):513-6. https://www.tandfonline.com/doi/abs/10.1179/acb.2009.087	Not reported in abstract/abstract not available
44.	Weinberger M, Keysary A, Sandbank J, Zaidenstein R, Itzhaki A, Strenger C, et al. **Fatal Rickettsia conorii subsp. israelensis infection, Israel**. Emerging Infectious Diseases 2008;14(5):821-4.	Molecular and immunohistochemical methods

	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2600240/	
45.	Tsiachris D, Deutsch M, Vassilopoulos D, Zafiropoulou R, Archimandritis AJ. **Sensorineural hearing loss complicating severe rickettsial diseases: report of two cases**. Journal of Infection 2008;56(1):74-6. https://www.sciencedirect.com/science/article/pii/S0163445307007864?via%3Dihub	Serology
46.	Tsai YS, Wu YH, Kao PT, Lin YC. **African tick bite fever**. Journal of the Formosan Medical Association 2008;107(1):73-6. https://www.sciencedirect.com/science/article/pii/S092966460860011X	Serology and DNA sequencing
47.	Leone S, De Marco M, Ghirga P, Nicastri E, Lazzari R, Narciso P. **Retinopathy in Rickettsia conorii infection: Case report in an immunocompetent host**. Infection 2008;36(4):384-6. https://link.springer.com/article/10.1007%2Fs15010-007-6291-9	Not reported in abstract/abstract not available
48.	Ergas D, Sthoeger MZ, Keysary A, Strenger C, Leitner M, Zimhony O. **Early diagnosis of severe Mediterranean spotted fever cases by nested-PCR detecting spotted fever Rickettsiae 17-kD common antigen gene**. Scandinavian Journal of Infectious Diseases 2008;40(11-12):965-7. https://www.tandfonline.com/doi/full/10.1080/00365540802400584	Nested-PCR assay and serology
49.	Colomba C, Saporito L, Colletti P, Mazzola G, Rubino R, Pampinella D, et al. **Atrial fibrillation in Mediterranean spotted fever**. Journal of Medical Microbiology 2008;57(Pt 11):1424-6.	IFA

5 Neoehrlichiosis (Candidatus Neoehrlichia mikurensis)

We found no diagnostic studies and five case studies/case series on Neoehrlichiosis (Candidatus Neoehrlichia Mikurensis). The search terms for Candidatus Neoehrlichia Mikurensis were quality assured to secure that all relevant terms had been used.

5.1 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Dutta S, Patel C, Sutton C, Genese F, Miller P, Asad R. **A ticking time bomb: A mysterious case of altered mental status**. Critical Care Medicine 2018;46 (Supplement 1):299. https://oce.ovid.com/article/00003246-201801001-00589/HTML	Serology
2.	Grankvist A, Andersson PO, Mattsson M, Sender M, Vaht K, Hoper L, et al. **Infections with the tick-borne bacterium "Candidatus Neoehrlichia mikurensis" mimic noninfectious conditions in patients with B cell malignancies or autoimmune diseases**. Clinical Infectious Diseases 2014;58(12):1716-22. https://academic.oup.com/cid/article/58/12/1716/2895431	Not reported in abstract/abstract not available
3.	Pekova S, Vydra J, Kabickova H, Frankova S, Haugvicova R, Mazal O, et al. **Candidatus Neoehrlichia mikurensis infection identified in 2 hematooncologic patients: benefit of molecular techniques for rare pathogen detection**. Diagnostic Microbiology & Infectious Disease 2011;69(3):266-70. https://www.sciencedirect.com/science/article/pii/S0732889310004426?via%3Dihub	16S rDNA sequencing and transmission electron microscopy
4.	von Loewenich FD, Geissdorfer W, Disque C, Matten J, Schett G, Sakka SG, et al. **Detection of "Candidatus Neoehrlichia mikurensis" in two patients with severe febrile illnesses: evidence for a European sequence variant**. Journal of Clinical Microbiology 2010;48(7):2630-5. https://jcm.asm.org/content/48/7/2630	16S rRNA and *groEL* gene sequencing
5.	Fehr JS, Bloemberg GV, Ritter C, Hombach M, Luscher TF, Weber R, et al. **Septicemia Caused by Tick-borne Bacterial Pathogen Candidatus Neoehrlichia mikurensis**. Emerging Infectious Diseases 2010;16(7):1127-9. https://wwwnc.cdc.gov/eid/article/16/7/09-1907_article	Serology

6 Babesiois (Babesia spp)

We found one systematic review, 27 diagnostic studies and 86 case studies/case series on babesiois (Babesia).

6.1 Systematic review

	Reference	Diagnostic test(s) studied
1.	Sanchez E, Vannier E, Wormser GP, Hu LT. **Diagnosis, treatment, and prevention of Lyme disease, Human Granulocytic Anaplasmosis, and Babesiosis** A Review. Jama-Journal of the American Medical Association 2016;315(16):1767-1777. https://jamanetwork.com/journals/jama/fullarticle/2516719	Several different methods studied

6.2 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Hanron AE, Billman ZP, Seilie AM, Chang M, Murphy SC. **Detection of Babesia microti parasites by highly sensitive 18S rRNA reverse transcription PCR**. Diagnostic Microbiology & Infectious Disease 2017;87(3):226-228. https://www.sciencedirect.com/science/article/pii/S0732889316304059	rt-PCR
2.	Primus S, Akoolo L, Schlachter S, Parveen N. Screening of patient blood samples for babesiosis using enzymatic assays. Ticks Tick-Borne Dis 2018;9(2):302-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6330027/	Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)
3.	Rozej-Bielicka W, Masny A, Golab E. **High-resolution melting PCR assay, applicable for diagnostics and screening studies, allowing detection and differentiation of several Babesia spp. infecting humans and animals**. Parasitol Res 2017;116(10):2671-2681. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5599466/	PCR
4.	Souza SS, Bishop HS, Sprinkle P, Qvamstrom Y. **Comparison of Babesia microti Real-Time Polymerase Chain Reaction Assays for Confirmatory Diagnosis of Babesiosis**. American Journal of Tropical Medicine and Hygiene 2016;95(6):1413-1416. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5154459/	rt-PCRvs. conventional PCR

5.	Simonetti A, Menis M, Kumar S, McKean S, Kelman JA, Worrall CM, et al. **Testing strategies for babesia microti in blood donors to reduce risk of transfusion-transmitted babesiosis in the United States**. Transfusion 2016;56 (Supplement 4):190A.	Not reported/abstract not available
6.	Chen MX, Ai L, Chen JH, Feng XY, Chen SH, Cai YC, et al. **DNA Microarray Detection of 18 Important Human Blood Protozoan Species**. PLoS Neglected Tropical Diseases [electronic resource] 2016;10(12):e0005160. http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0005160	Novel DNA microarray system vs. microscopy and PCR data
7.	Aase A, Hajdusek O, Oines O, Quarsten H, Wilhelmsson P, Herstad TK, et al. **Validate or falsify: Lessons learned from a microscopy method claimed to be useful for detecting Borrelia and Babesia organisms in human blood**. Infectious Diseases 2016;48(6):411-419. https://www.tandfonline.com/doi/abs/10.3109/23744235.2016.1144931	A modified microscopy protocol (the LM-method) vs. PCR and serology
8.	Levin AE, Williamson PC, Bloch EM, Clifford J, Cyrus S, Shaz BH, et al. **Serologic screening of United States blood donors for Babesia microti using an investigational enzyme immunoassay**. Transfusion 2016;56(7):1866-1874. https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.13618	Investigational enzyme immunoassay (EIA)
9.	Wang G, Villafuerte P, Zhuge J, Visintainer P, Wormser GP. **Comparison of a quantitative PCR assay with peripheral blood smear examination for detection and quantitation of Babesia microti infection in humans**. Diagnostic Microbiology & Infectious Disease 2015;82(2):109-113. https://linkinghub.elsevier.com/retrieve/pii/S0732-8893(15)00076-0	rt-PCR and blood smear
10.	Racsa LD, Gander RM, Southern PM, McElvania TeKippe E, Doern C, Luu HS. **Detection of intracellular parasites by use of the CellaVision DM96 analyzer during routine screening of peripheral blood smears**. Journal of Clinical Microbiology 2015;53(1):167-171. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4290916/	CellaVision DM96 digital hematology analyzer vs. routine red blood cell morphology scan
11.	Bish EK, Moritz ED, El-Amine H, Bish DR, Stramer SL. **Cost-effectiveness of Babesia microti antibody and nucleic acid blood donation screening using results from prospective investigational studies**. Transfusion 2015;55(9):2256-2271. https://onlinelibrary.wiley.com/doi/pdf/10.1111/trf.13136	Antibody and PCR assays

12.	Wang G, Wormser GP, Zhuge J, Villafuerte P, Ip D, Zeren C, et al. **Utilization of a real-time PCR assay for diagnosis of Babesia microti infection in clinical practice**. Ticks & tick-borne Diseases 2015;6(3):376-382. https://www.sciencedirect.com/science/article/pii/S1877959X15000382?via%3Dihub	PCR and. blood smear examination
13.	Wilson M, Glaser KC, Adams-Fish D, Boley M, Mayda M, Molestina RE. **Development of droplet digital PCR for the detection of Babesia microti and Babesia duncani**. Experimental Parasitology 2015;149:24-31. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4314376/	Droplet digital PCR (ddPCR) assays
14.	Verma NK, Zheng H, Puri A, Bradley C, Kumar S. **Genomics approach to identify the immunodominant babesia microti antigens for the diagnostics and vaccine use**. American Journal of Tropical Medicine and Hygiene 2015;93 (4 Supplement):212. http://www.ajtmh.org/docserver/fulltext/14761645/93/4_Suppl/501.pdf?expires=1548329903&id=id&accname=guest&checksum=DDDF954D093761493E370FEF26708DEA	Not reported/abstract not available
15.	Levin AE, Williamson PC, Bloch E, Shaz BH, Kessler DA, Gorlin JB, et al. **Screening United States blood donors for babesia microti with an investigational EIA**. Transfusion 2015;3):43A-44A. https://onlinelibrary.wiley.com/doi/10.1111/trf.13294	Investigational enzyme immunoassay (EIA), immunofluorescence assay (IFA), blood smear, PCRs, and Western Blot.
16.	Winkelman V, Cyrus S, Hislop S, Levin AE, Telford SR, Williamson PC, et al. **Development and Validation of an IFA Protocol for Babesia microti Antibody Detection**. Transfusion 2014;54:208a-208a. https://onlinelibrary.wiley.com/doi/10.1111/trf.12845	IFA
17.	Leiby DA, Johnson ST, Won KY, Nace EK, Slemenda SB, Pieniazek NJ, et al. **A longitudinal study of Babesia microti infection in seropositive blood donors**. Transfusion 2014;54(9):2217-2225. https://onlinelibrary.wiley.com/doi/10.1111/trf.12622	Polymerase chain reaction (PCR) analysis (at two laboratories), hamster inoculation, and blood-smear examination
18.	Levin AE, Williamson PC, Erwin JL, Cyrus S, Bloch EM, Shaz BH, et al. **Determination of Babesia microti seroprevalence in blood donor populations using an investigational enzyme immunoassay**. Transfusion 2014;54(9):2237-2244. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4163072/	investigational enzyme immunoassay (EIA) vs. immunofluorescent assay (IFA), polymerase chain reaction (PCR) on red blood cell lysates, and peripheral blood smear examination

19.	Rollend L, Bent SJ, Krause PJ, Usmani-Brown S, Steeves TK, States SL, et al. **Quantitative PCR for detection of Babesia microti in Ixodes scapularis ticks and in human blood**. Vector Borne & Zoonotic Diseases 2013;13(11):784-790. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3822370/	Quantitative PCR (qPCR) assay (BabMq18) va. two nonquantitative PCR assays
20.	Priest JW, Moss DM, Won K, Todd CW, Henderson L, Jones CC, et al. **Multiplex assay detection of immunoglobulin G antibodies that recognize Babesia microti antigens**. Clinical & Vaccine Immunology: CVI 2012;19(9):1539-1548. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3428400/	Multiplex bead format assay (MBA) vs. assay using a truncated recombinant BMN1-17 construct
21.	Gabrielli S, Galuppi R, Marcer F, Marini C, Tampieri MP, Moretti A, et al. **Development of culture-based serological assays to diagnose Babesia divergens infections**. Vector Borne & Zoonotic Diseases 2012;12(2):106-110. https://www.liebertpub.com/doi/abs/10.1089/vbz.2011.0706?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed	ELISA, IFA, WB
22.	Erwin JL, Ni X, Wang H, Krueger NX, Telford SR, Krause PJ, et al. **Sensitive and specific peptide based ELISA for detection of antibodies to babesia microti**. Transfusion 2012;3):209A. https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1537-2995.2012.03833_1.x	Peptide-based microwell ELISA vs blood smear or PCR
23.	Teal AE, Habura A, Ennis J, Keithly JS, Madison-Antenucci S. **A new real-time PCR assay for improved detection of the parasite Babesia microti**. Journal of Clinical Microbiology 2012;50(3):903-908. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3295123/	Real-time PCR assay targeting the 18S rRNA gene vs microscopic examination?
24.	Ohmori S, Kawai A, Takada N, Saito-Ito A. **Development of real-time PCR assay for differential detection and quantification for multiple Babesia microti-genotypes**. Parasitology International 2011;60(4):403-409. https://www.sciencedirect.com/science/article/pii/S1383576911000912?via%3Dihub	Real-time PCR assay
25.	Imugen, Cross ANR, Memorial Blood Centers M, Center RIB. **Babesia Testing in Blood Donors**. https://ClinicalTrials.gov/show/NCT01528449 ; 2011.	Real-time (PCR) and Indirect Flourescent Antibody (IFA) Assays
26.	Devine P, Berardi V, Molloy P, Brissette E, Hewins M, Young C. **Babesia microti tests for blood donor screening**. Transfusion 2011;3):204A. https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1537-2995.2011.03301_1.x	rt-PCR and automatiable array IFA .
27.	Duh D, Jelovsek M, Avsic-Zupanc T. **Evaluation of an indirect fluorescence immunoassay for the detection of serum antibodies against Babesia divergens in humans**. Parasitology 2007;134(Pt 2):179-185. https://www.cambridge.org/core/journals/parasitology/article/evaluation-of-an-indirect-fluorescence-immunoassay-for-the-detection-of-serum-antibodies-against-babesia-divergens-in-humans/383903F4DAC8D7E22D09F300A83B4E0E	In-house IFA vs. a commercially available IFA

6.3 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Bhardwaj A, Malsin E, Srinivasan K, Fritz J, Gutsche J. **Venovenous ecmo use in babesiosisassociated ards: A success story**. Critical Care Medicine 2018;46 (Supplement 1):313. https://journals.lww.com/ccmjournal/Citation/2018/01001/654__VENOVENOUS_ECMO_USE_IN_BABESIOSIS_ASSOCIATED.618.aspx	Peripheral blood smear
2.	Scott JD. **First record of locally acquired human babesiosis in Canada caused by Babesia duncani: a case report**. SAGE Open Medical Case Reports 2017;5:2050313X17725645. https://journals.sagepub.com/doi/full/10.1177/2050313X17725645	IFA and Babesia fluorescent in situ hybridization (FISH) test
3.	Paparone P, Paparone PW. **Variable clinical presentations of babesiosis: A case series**. Nurse Practitioner 2017;42(11):1-7. https://insights.ovid.com/pubmed?pmid=29040182	Not reported in abstract/abstract not available
4.	O'Connell S, Lyons C, Abdou M, Patowary R, Aslam S, Kinsella N, et al. **Splenic dysfunction from celiac disease resulting in severe babesiosis**. Ticks and Tick-borne Diseases 2017;8(4):537-9. https://www.sciencedirect.com/science/article/pii/S1877959X17301139?via%3Dihub	Not reported in abstract/abstract not available
5.	Munshi AA, Latimer B, Bosse C. **Acute respiratory distress syndrome complicating babesiosis and lyme coinfection**. American Journal of Respiratory and Critical Care Medicine Conference: American Thoracic Society International Conference, ATS 2017;195. https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2017.195.1_MeetingAbstracts.A5867	Peripheral blood smear, IgG and IgM
6.	Leparc GF. **Transfusion-transmitted babesiosis outside an endemic area: A case report**. Transfusion 2017;57 (Supplement 3):204A. https://onlinelibrary.wiley.com/doi/10.1111/trf.14286	PCR, serology

7.	Lehrke HD, Winters JL. **Red cell exchange for a case of babesiosis**. Journal of Clinical Apheresis 2017;32(4):271-2. https://onlinelibrary.wiley.com/doi/abs/10.1002/jca.21495	Not reported in abstract/abstract not available
8.	LeBel DP, 2nd, Moritz ED, O'Brien JJ, Lazarchick J, Tormos LM, Duong A, et al. **Cases of transfusion-transmitted babesiosis occurring in nonendemic areas: a diagnostic dilemma**. Transfusion 2017;57(10):2348-54. https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.14246	Not reported in abstract/abstract not available
9.	Go SA, Phuoc VH, Eichenberg SE, Temesgen Z, Beckman TJ. **Babesia microti infection and hemophagocytic lymphohistiocytosis in an immunocompetent patient**. International Journal of Infectious Diseases 2017;65:72-4. https://linkinghub.elsevier.com/retrieve/pii/S1201-9712(17)30251-5	Not reported in abstract/abstract not available
10.	Burgess MJ, Rosenbaum ER, Pritt BS, Haselow DT, Ferren KM, Alzghoul BN, et al. **Possible transfusion-transmitted Babesia divergens-like/MO-1 infection in an Arkansas patient**. Clinical Infectious Diseases 2017;64(11):1622-5. https://academic.oup.com/cid/article/64/11/1622/3067352	Not reported in abstract/abstract not available
11.	Alquist CR, Szczepiorkowski ZM, Dunbar N. **Babesia parasitemia rebound after red blood cell exchange**. Journal of Clinical Apheresis 2017;32(4):276-8. https://onlinelibrary.wiley.com/doi/abs/10.1002/jca.21492	Peripheral blood smear
12.	Akel T, Mobarakai N. **Hematologic manifestations of babesiosis**. Annals of Clinical Microbiology & Antimicrobials 2017;16(1):6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5310009/	Peripheral blood smear, PCR
13.	Strakl G, Gruskovnjak J, Pal E, Weiss VC. **Case report: First confirmed case of human babesiosis in Slovenia**. Clinical Chemistry and Laboratory Medicine 2016;54 (9):eA151. https://www.degruyter.com/view/j/cclm.2016.54.issue-9/cclm-2016-0624/cclm-2016-0624.xml	Peripheral blood smear
14.	Merino A. **Blood film findings in severe babesiosis**. British Journal of Haematology 2016;172(6):839. https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.13845	Peripheral blood smear
15.	Jablonska J, Zarnowska-Prymek H, Stanczak J, Kozlowska J, Wiercinska-Drapalo A. **Symptomatic co-infection with Babesia microti and Borrelia burgdorferi in patient after international exposure; a challenging case in Poland**. Annals of Agricultural & Environmental Medicine 2016;23(2):387-9. http://www.aaem.pl/Symptomatic-co-infection-with-Babesia-microti-nand-Borrelia-burgdorferi-in-patient,72435,0,2.html	Not reported in abstract/abstract not available

16.	Gulersen M, Brost BC, Bobrovnikov V, Bornstein E. **Acute babesiosis in pregnancy**. Obstetrics and Gynecology 2016;128(1):197-200. https://insights.ovid.com/pubmed?pmid=27275801	Peripheral blood smear
17.	de Ramon C, Cid J, Rodriguez-Tajes S, Alvarez-Martinez MJ, Valls ME, Fernandez J, et al. **Severe Babesia microti infection in an American immunocompetent patient diagnosed in Spain**. Transfusion & Apheresis Science 2016;55(2):243-4. https://www.trasci.com/article/S1473-0502(16)30099-4/fulltext	Giemsa-stained peripheral blood smears, optical microscopy, PCR
18.	Bade NA, Yared JA. **Unexpected babesiosis in a patient with worsening anemia after allogeneic hematopoietic stem cell transplantation**. Blood 2016;128(7):1019. http://www.bloodjournal.org/content/128/7/1019?sso-checked=true	Peripheral blood smear, PCR
19.	Arsuaga M, Gonzalez LM, Lobo CA, de la Calle F, Bautista JM, Azcarate IG, et al. **First Report of Babesia microti-Caused Babesiosis in Spain**. Vector Borne & Zoonotic Diseases 2016;16(10):677-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5065027/	PCR and IFA
20.	Alkhawam H, Zaiem F, Lee S, Fabisevich M, Ashraf A. **Sever symptomatic babesiosis co-infection with lyme disease**. Journal of Investigative Medicine 2016;64 (4):956. https://jim.bmj.com/content/64/4/956.1	Peripheral blood smear, serology
21.	Al Zoubi M, Kwak T, Patel J, Kulkarni M, Kallal CA. **Atypical challenging and first case report of babesiosis in Ecuador**. IDCases 2016;4:15-7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4802672/	Peripheral blood smear, PCR
22.	Al Soub H, Al Maslamani M, Ahmedullah HS, Shawkat A, Ibrahim FA, Kanbar NA. **First case of babesiosis in Qatar: Case report**. Jordan Medical Journal 2016;50(3):161-7. https://www.researchgate.net/publication/308120800_First_case_of_babesiosis_in_Qatar_Case_report	Blood film
23.	Welc-Faleciak R, Pawelczyk A, Radkowski M, Pancewicz SA, Zajkowska J, Sinski E. **First report of two asymptomatic cases of human infection with Babesia microti (Franca, 1910) in Poland**. Annals of Agricultural and Environmental Medicine 2015;22(1):51-4. http://www.aaem.pl/First-report-of-two-asymptomatic-cases-of-human-infection-with-Babesia-microti-Franca,72231,0,2.html	Molecular methods (PCR, R-T PCR, DNA sequencing and phylogenetic analysis)

24.	Warren T, Lau R, Ralevski F, Rau N, Boggild AK. **Fever in a visitor to Canada: a case of mistaken identity**. Journal of Clinical Microbiology 2015;53(5):1783-5. https://jcm.asm.org/content/53/5/1783	Peripheral blood smears, PCR
25.	Surra ND, Jesus JE. **The anemic and thrombocytopenic febrile neonate**. Journal of Emergency Medicine 2015;48(6):675-8. https://linkinghub.elsevier.com/retrieve/pii/S0736-4679(15)00022-0	Peripheral blood smear
26.	Shatzel JJ, Donohoe K, Chu NQ, Garratty G, Mody K, Bengtson EM, et al. **Profound autoimmune hemolysis and Evans syndrome in two asplenic patients with babesiosis**. Transfusion 2015;55(3):661-5. https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.12901	Not reported in abstract/abstract not available
27.	Morch K, Holmaas G, Frolander PS, Kristoffersen EK. **Severe human Babesia divergens infection in Norway**. International Journal of Infectious Diseases 2015;33:37-8. https://linkinghub.elsevier.com/retrieve/pii/S1201-9712(14)01752-4	Giemsa-stained blood smears
28.	LeBel DP, Lazarchick J, Squires JE. **Transfusion-transmitted babesiosis; a diagnostic dilemma**. Transfusion 2015;3):185A. https://onlinelibrary.wiley.com/doi/abs/10.1111/trf.14246	Peripheral blood smear
29.	Jiang JF, Zheng YC, Jiang RR, Li H, Huo QB, Jiang BG, et al. **Epidemiological, clinical, and laboratory characteristics of 48 cases of "Babesia venatorum" infection in China: a descriptive study**. The Lancet Infectious Diseases 2015;15(2):196-203. https://linkinghub.elsevier.com/retrieve/pii/S1473-3099(14)71046-1	"PCR followed by sequencing, microscopic identification, or isolation by animal inoculation, or both"
30.	Jagtap P, Hoskote SS, Ohoro J, Guru PK. **Successful management of fulminant babesiosis with red blood cell exchange transfusion**. American Journal of Respiratory and Critical Care Medicine Conference: American Tho racic Society International Conference, ATS 2015;191(MeetingAbstracts). https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2015.191.1_MeetingAbstracts.A1666	Serology, PCR
31.	Forrester K, Franco LG, Postelnicu R, Jacobs REA. **Haematologic complications from human babesiosis: A case report**. New Microbes and New Infections 2015;8:148-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4877399/	Not reported in abstract/abstract not available

32.	Cunha BA, Raza M, Schmidt A. **Highly elevated serum ferritin levels are a diagnostic marker in babesiosis**. Clinical Infectious Diseases 2015;60(5):827-9. https://academic.oup.com/cid/article/60/5/827/292078	Not reported in abstract/abstract not available
33.	Sun Y, Li SG, Jiang JF, Wang X, Zhang Y, Wang H, et al. **Babesia venatorum Infection in Child, China**. Emerging Infectious Diseases 2014;20(5):896-7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4012784/	Not reported in abstract/abstract not available
34.	Paparini A, Senanayake SN, Ryan UM, Irwin PJ. **Molecular confirmation of the first autochthonous case of human babesiosis in Australia using a novel primer set for the beta-tubulin gene**. Experimental Parasitology 2014;141:93-7. https://www.sciencedirect.com/science/article/pii/S0014489414000381?via%3Dihub	Novel PCR-based assay
35.	Panduranga V, Kumar A. **Severe babesiosis presenting as acute respiratory distress syndrome in an immunocompetent patient**. Connecticut Medicine 2014;78(5):289-91. https://www.ncbi.nlm.nih.gov/pubmed/24974563	Wright-Giemsa stained thin blood smear
36.	Manohar A, Yankovich A, Gerasim S, Goldsmith D. **Tick-talk, tick-talk: When a fever, headache and stiff neck isn't meningitis**. Journal of General Internal Medicine 2014;1):S455. https://link.springer.com/content/pdf/10.1007%2Fs11606-014-2834-9.pdf	Peripheral blood smear
37.	Lutz JE, DeBess EE, Bryan BB, Rose B, Xayavong MV, Henderson LL, et al. **The first reported case of babesiosis in a resident of oregon**. American Journal of Tropical Medicine and Hygiene 2014;1):30. https://www.ajtmh.org/content/journals/10.4269/ajtmh.2014.91.5_Suppl_1.astmh_14_abstracts_1_250	Molecular and serologic analyses
38.	Luckett R, Rodriguez W, Katz D. **Babesiosis in pregnancy**. Obstetrics & Gynecology 2014;124(2 Pt 2 Suppl 1):419-22. https://insights.ovid.com/pubmed?pmid=25004307	Not reported in abstract/abstract not available
39.	Bullard JM, Ahsanuddin AN, Perry AM, Lindsay LR, Iranpour M, Dibernardo A, et al. **The first case of locally acquired tick-borne Babesia microti infection in Canada**. The Canadian Journal of Infectious Diseases & Medical Microbiology 2014;25(6):e87-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4277163/	Not reported in abstract/abstract not available
40.	Poisnel E, Ebbo M, Berda-Haddad Y, Faucher B, Bernit E, Carcy B, et al. **Babesia microti: an unusual travel-related disease**. BMC Infectious Diseases 2013;13:99. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3598249/	Not reported in abstract/abstract not available

41.	Milner CP, Elkins S. **It's all about the bite: A case of babesiosis presenting as hemolysis**. Journal of Investigative Medicine 2013;61 (2):406. https://jim.bmj.com/content/61/2/373#article-bottom	Blood smear, PCR
42.	Maolv VA, Tokmalaev AK, Erovichenkov AA, Tsvetkova NA, Sadykova VD, Smetanina SV, et al. **Human babesiasis . Russian**. Terapevticheskii arkhiv 2013;85(11):62-6. https://www.ncbi.nlm.nih.gov/pubmed/24432602	Not reported in abstract/abstract not available
43.	Ling C, Chen Z, Sun Q, Meng Q, Fan JF, Liu XR, et al. **Rhabdomyolysis, anemia and ARF-babesia infection**. Pediatric Nephrology 2013;28 (8):1414-5. https://link.springer.com/article/10.1007%2Fs00467-013-2518-4	Haematological examination of peripheral blood smears
44.	Leinwand JC, Arroyo JP, Solomon D, Kaplan LJ. **Babesia microti infection presenting as acute splenic laceration**. Surgical Infections 2013;14(4):412-4. https://www.liebertpub.com/doi/abs/10.1089/sur.2012.137?rfr_dat=cr_pub%3Dpubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&journalCode=sur	Not reported in abstract/abstract not available
45.	Kathman D, Nesanelis D, Fitzgibbons C. **A rare cause of posttransfusion hemolytic anemia**. Chest Conference: CHEST 2013;144(4 MEETING ABSTRACT). https://journal.chestnet.org/article/S0012-3692(16)42830-8/pdf	Blood smear, PCR
46.	Holler JG, Roser D, Nielsen HV, Eickhardt S, Chen M, Lester A, et al. **A case of human babesiosis in Denmark**. Travel Medicine & Infectious Disease 2013;11(5):324-8. https://www.sciencedirect.com/science/article/pii/S1477893913000963?via%3Dihub	Not reported in abstract/abstract not available
47.	Acosta ME, Ender PT, Smith EM, Jahre JA. **Babesia microti infection, eastern Pennsylvania, USA**. Emerging Infectious Diseases 2013;19(7):1105-7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3713976/	Not reported in abstract/abstract not available
48.	Yao LN, Ruan W, Zeng CY, Li ZH, Zhang X, Lei YL, et al. **Pathogen identification and clinical diagnosis for one case infected with Babesia**. Chung-Kuo Chi Sheng Chung Hsueh Yu Chi Sheng Chung Ping Tsa Chih Chinese Journal of Parasitology & Parasitic Diseases 2012;30(2):118-21. https://www.ncbi.nlm.nih.gov/pubmed/22908812	Peripheral blood smear and PCR

49.	Singh PP, Das S, Cherian SV, Singh P, Lenox R. **Adult respiratory distress syndrome secondary to babesiosis**. American Journal of Respiratory and Critical Care Medicine Conference: American Thoracic Society International Conference, ATS 2012;185(MeetingAbstracts). https://www.researchgate.net/publication/269233620_Adult_Respiratory_Distress_Syndrome_Secondary_To_Babesiosis	Not reported in abstract/abstract not available
50.	Senanayake SN, Paparini A, Latimer M, Andriolo K, Dasilva AJ, Wilson H, et al. **First report of human babesiosis in Australia**. Medical Journal of Australia 2012;196(5):350-2. https://www.mja.com.au/journal/2012/196/5/first-report-human-babesiosis-australia	Not reported in abstract/abstract not available
51.	Papari M, Phillips M, Lynn C, Soyemi K, Hoferka Jensen S, Chugh R, et al. **Investigation of a case of babesia microti infection in 2011 in a multiply transfused patient in Illinois**. Transfusion 2012;3):210A. https://onlinelibrary.wiley.com/doi/10.1111/trf.12401	Not reported in abstract/abstract not available
52.	Kumar P, Marshall BC, deBlois G, Koch WC. **A cluster of transfusion-associated babesiosis in extremely low birthweight premature infants**. Journal of Perinatology 2012;32(9):731-3. https://www.nature.com/articles/jp201233	Not reported in abstract/abstract not available
53.	Joseph JT, Purtill K, Wong SJ, Munoz J, Teal A, Madison-Antenucci S, et al. **Vertical transmission of Babesia microti, United States**. Emerging Infectious Diseases 2012;18(8):1318-21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3414010/	PCR
54.	Jaber R, Brennan M. **Getting the patient out of the woods - Near death from babesiosis in an elder**. Journal of the American Geriatrics Society 2012;4):S77. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1532-5415.2012.04000.x	Not reported in abstract/abstract not available
55.	Fuller A, Manitta J, Marks R, Tencic S, Gordon CL. **First reported case of imported human Babesia microti infection in Australia**. Pathology 2012;44(6):580-2. https://www.pathologyjournal.rcpa.edu.au/article/S0031-3025(16)32488-6/fulltext	Not reported in abstract/abstract not available
56.	DiLorenzo M, Agus B. **Symptomatic babesiosis in systemic lupus erythematosus: report of a case and review of the literature**. Bulletin of the NYU Hospital for Joint Diseases 2012;70(2):124-6. https://www.ncbi.nlm.nih.gov/pubmed/22892003	Not reported in abstract/abstract not available

57.	Danilchuk B, Leclair SJ. **Hemolytic anemia accelerated by Babesia spp. infection in splenectomized patient**. Clinical Laboratory Science 2012;25(4):194-8. http://clsjournal.ascls.org/content/25/4/194	Molecular DNA testing, peripheral blood smear
58.	Bogoch, II, Davis BT, Hooper DC. **Severe babesiosis in a patient treated with a tumor necrosis factor alpha antagonist**. Clinical Infectious Diseases 2012;54(8):1215-6. https://academic.oup.com/cid/article/54/8/1215/367050	Not reported in abstract/abstract not available
59.	Bloch EM, Herwaldt BL, Leiby DA, Shaieb A, Herron RM, Chervenak M, et al. **The third described case of transfusion-transmitted Babesia duncani**. Transfusion 2012;52(7):1517-22. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1537-2995.2011.03467.x	Blood smear, IFA and PCR
60.	Andric B, Golubovic M, Terzic D, Dupanovic B, Icevic M. **First diagnostic cases of human babesiosis in Montenegro**. Brazilian Journal of Infectious Diseases 2012;16(5):498-9. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-86702012000500022	Not reported in abstract/abstract not available
61.	Wudhikarn K, Perry EH, Kemperman M, Jensen KA, Kline SE. **Transfusion-transmitted Babesiosis in an Immunocompromised Patient: A Case Report and Review**. American Journal of Medicine 2011;124(9):800-5. https://linkinghub.elsevier.com/retrieve/pii/S0002-9343(11)00247-6	Peripheral blood smears, confirmed by PCR
62.	Van Vugt M, Wetsteyn JC, Haverkort M, Kolader M, Verhaar N, Spanjaard L, et al. **New England souvenirs**. Journal of Travel Medicine 2011;18(6):425-6. https://academic.oup.com/jtm/article/18/6/425/1806637	Not reported in abstract/abstract not available
63.	Martinot M, Zadeh MM, Hansmann Y, Grawey I, Christmann D, Aguillon S, et al. **Babesiosis in immunocompetent patients, Europe**. Emerging Infectious Diseases 2011;17(1):114-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3204631/	Peripheral blood smears, PCR
64.	Chiang E, Haller N. **Babesiosis: an emerging infectious disease that can affect those who travel to the northeastern United States**. Travel Medicine & Infectious Disease 2011;9(5):238-42. https://www.sciencedirect.com/science/article/pii/S1477893911000676?via%3Dihub	Peripheral blood smears, PCR
65.	Ramharter M, Walochnik J, Lagler H, Winkler S, Wernsdorfer WH, Stoiser B, et al. **Clinical and molecular characterization of a near fatal case of human babesiosis in Austria**. Journal of Travel Medicine 2010;17(6):416-8.	PCR and sequence analysis

	https://academic.oup.com/jtm/article/17/6/416/1844932	
66.	McNamara R, Van Der Velde J, Meeke R. **Babesiosis-an unusual cause of acute confusion in an elderly man**. European Geriatric Medicine 2010;1):S158. https://www.sciencedirect.com/science/article/pii/S1878764910001579?via%3Dihub	Not reported in abstract/abstract not available
67.	Linden JV, Olkowska D, Grima KM, Manning ML. **A series of 23 transfusion-associated babesiosis cases**. Transfusion 2010;2):40A. https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1537-2995.2010.02833_1.x	Not reported in abstract/abstract not available
68.	Husseinzadeh H, Mehta P, Suri S. **A case of chronic fevers in a peripatetic patient**. Journal of Hospital Medicine 2010;1):146. https://onlinelibrary.wiley.com/doi/abs/10.1002/jhm.709	Thick and thin peripheral blood smears
69.	Cullen G, Sands BE, Yajnik V. **Babesiosis in a patient on infliximab for Crohn's disease**. Inflammatory Bowel Diseases 2010;16(8):1269-70. https://academic.oup.com/ibdjournal/article-abstract/16/8/1269/4628408?redirectedFrom=fulltext	Not reported in abstract/abstract not available
70.	Browne S, Ryan Y, Goodyer M, Gilligan O. **Fatal babesiosis in an asplenic patient**. British Journal of Haematology 2010;148(4):494. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2141.2009.07829.x	Wright or Giemsa stained thin blood smear
71.	Aderinboye O, Syed SS. **Congenital babesiosis in a four-week-old female infant**. Pediatric Infectious Disease Journal 2010;29(2):188. https://insights.ovid.com/pubmed?pmid=20118748	Not reported in abstract/abstract not available
72.	Abbas S. **A History is worth a million dollar workup**. Journal of Hospital Medicine 2010;(1):111. https://onlinelibrary.wiley.com/doi/abs/10.1002/jhm.709	Serology, thin blood smear
73.	Zhao Y, Love KR, Hall SW, Beardell FV. **A fatal case of transfusion-transmitted babesiosis in the State of Delaware**. Transfusion 2009;49(12):2583-7. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1537-2995.2009.02454.x	Peripheral blood smears, PCR and IFA
74.	Sethi S, Alcid D, Kesarwala H, Tolan RW, Jr. **Probable congenital babesiosis in infant, new jersey, USA**. Emerging Infectious Diseases 2009;15(5):788-91.	Peripheral blood smears, serology

	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2687033/	
75.	Rawling RA, Strouse K, Granato PA. **Borrelia burgdorferi and Babesia microti Coinfection in a 79-Year-Old Camper**. Clinical Microbiology Newsletter 2009;31(5):37-9. https://www.cabdirect.org/cabdirect/abstract/20093079211	Not reported in abstract/abstract not available
77.	Haselbarth K, Kurz M, Hunfeld KP, Krieger G. **Babesiosis in an immunocompromised german patient. German**. Medizinische Klinik 2008;103(2):104-7. https://link.springer.com/article/10.1007%2Fs00063-008-1014-2	Peripheral blood smears, PCR, serology
78.	Florescu D, Sordillo PP, Glyptis A, Zlatanic E, Smith B, Polsky B, et al. **Splenic infarction in human babesiosis: two cases and discussion**. Clinical Infectious Diseases 2008;46(1):e8-11. https://academic.oup.com/cid/article/46/1/e8/339601	Not reported in abstract/abstract not available
79.	Cunha BA, Cohen YZ, McDermott B. **Fever of unknown origin (FUO) due to babesiosis in a immunocompetent host**. Heart & Lung 2008;37(6):481-4. https://linkinghub.elsevier.com/retrieve/pii/S0147-9563(08)00019-8	Peripheral blood smears
80.	Bouree P, Resende P, Gagnepain-Lacheteau A, Marsaudon E. **An underestimated protozoiasis: Babesiosis**. Antibiotiques 2008;10(2):61-8.	Giemsa-stained thin blood smear, serology
81.	Schaller JL, Burkland GA, Langhoff PJ. **Are various Babesia species a missed cause for hypereosinophilia? A follow-up on the first reported case of imatinib mesylate for idiopathic hypereosinophilia**. Medgenmed [Computer File]: Medscape General Medicine 2007;9(1):38. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1925019/	Not reported in abstract/abstract not available
82.	Kim JY, Cho SH, Joo HN, Tsuji M, Cho SR, Park IJ, et al. **First case of human babesiosis in Korea: detection and characterization of a novel type of Babesia sp. (KO1) similar to ovine babesia**. Journal of Clinical Microbiology 2007;45(6):2084-7. https://jcm.asm.org/content/45/6/2084.long	Peripheral blood smear and PCR
83.	Hildebrandt A, Hunfeld KP, Baier M, Krumbholz A, Sachse S, Lorenzen T, et al. **First confirmed autochthonous case of human Babesia microti infection in Europe**. European Journal of Clinical Microbiology & Infectious Diseases 2007;26(8):595-601. https://link.springer.com/article/10.1007%2Fs10096-007-0333-1	PCR, IFA

84.	Haselbarth K, Tenter AM, Brade V, Krieger G, Hunfeld KP. **First case of human babesiosis in Germany - Clinical presentation and molecular characterisation of the pathogen**. Ijmm International Journal of Medical Microbiology 2007;297(3):197-204. https://linkinghub.elsevier.com/retrieve/pii/S1438-4221(07)00016-1	Peripheral blood smears and PCR
85.	Dodd JD, Aquino SL, Sharma A. **Babesiosis: CT and hematologic findings**. Journal of Thoracic Imaging 2007;22(3):271-3. https://insights.ovid.com/pubmed?pmid=17721341	Not reported in abstract/abstract not available
86.	Cunha BA, Nausheen S, Szalda D. **Pulmonary complications of babesiosis: case report and literature review**. European Journal of Clinical Microbiology & Infectious Diseases 2007;26(7):505-8. https://link.springer.com/article/10.1007%2Fs10096-007-0325-1	Not reported in abstract/abstract not available

7 Hard tick relapsing fever (Borrelia miyamotoi)

We found four diagnostic studies and eleven case studies/case series on hard tick relapsing fever (Borrelia Miyamotoi).

7.1 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Jahfari S, Sarksyan DS, Kolyasnikova NM, Hovius JW, Sprong H, Platonov AE. **Evaluation of a serological test for the diagnosis of Borrelia miyamotoi disease in Europe**. Journal of Microbiological Methods 2017;136:11-16. https://www.sciencedirect.com/science/article/pii/S0167701217300532?via%3Dihub	Serological test using a fragment of glycerophosphodiester phosphodiesterase (GlpQ) as an antigen va. SV PCR

2.	Molloy PJ, Weeks KE, Todd B, Wormser GP. **Seroreactivity to the C6 Peptide in Borrelia Miyamotoi Infections Occurring in the Northeastern United States**. Clinical Infectious Diseases 2017;15:15. https://academic.oup.com/cid/article-abstract/66/9/1407/4631884?redirectedFrom=fulltext	FDA-approved C6 peptide enzyme-linked immuno-sorbent assay (C6 ELISA) currently used to diagnose Lyme disease
3.	Koetsveld J, Kolyasnikova NM, Wagemakers A, Toporkova MG, Sarksyan DS, Oei A, et al. **Development and optimization of an in vitro cultivation protocol allows for isolation of Borrelia miyamotoi from patients with hard tick-borne relapsing fever**. Clinical Microbiology & Infection 2017;23(7):480-484. https://www.sciencedirect.com/science/article/pii/S1198743X17300186	Blood culture
4.	Lee SH, Vigliotti JS, Vigliotti VS, Jones W, Moorcroft TA, Lantsman K. **DNA sequencing diagnosis of off-season spirochetemia with low bacterial density in Borrelia burgdorferi and Borrelia miyamotoi infections**. International Journal of Molecular Sciences 2014;15(7):11364-11386. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4139787/	PCR

7.2 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Yamano K, Ito T, Kiyanagi K, Yamazaki H, Sugawara M, Saito T, et al. **Case report: Clinical features of a case of suspected borrelia miyamotoi disease in Hokkaido, Japan**. American Journal of Tropical Medicine and Hygiene 2017;97(1):84-7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5508891/	Serology
2.	Oda R, Kutsuna S, Sekikawa Y, Hongo I, Sato K, Ohnishi M, et al. **The first case of imported Borrelia miyamotoi disease concurrent with Lyme disease**. Journal of Infection & Chemotherapy 2017;23(5):333-5. https://linkinghub.elsevier.com/retrieve/pii/S1341-321X(17)30007-7	Serology
3.	Fiorito TM, Reece R, Flanigan TP, Silverblatt FJ. **Borrelia miyamotoi Polymerase Chain Reaction Positivity on a Tick-Borne Disease Panel in an Endemic Region of Rhode Island: A Case Series**. Infectious Diseases in Clinical Practice 2017;25(5):250-4. https://www.researchgate.net/publication/317172502_Borrelia_miyamotoi_Polymerase_Chain_Reaction_Positivity_on_a_Tick-Borne_Disease_Panel_in_an_Endemic_Region_of_Rhode_Island_A_Case_Series	Whole blood PCR

4.	Sudhindra P, Wang G, Schriefer ME, McKenna D, Zhuge J, Krause PJ, et al. **Insights into Borrelia miyamotoi infection from an untreated case demonstrating relapsing fever, monocytosis and a positive C6 Lyme serology**. Diagnostic Microbiology & Infectious Disease 2016;86(1):93-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4993640/	PCR and serology
5.	Krause PJ, Schwab J, Narasimhan S, Brancato J, Xu G, Rich SM. **Hard Tick Relapsing Fever Caused by Borrelia miyamotoi in a Child**. Pediatric Infectious Disease Journal 2016;35(12):1352-4. https://journals.lww.com/pidj/Abstract/2016/12000/Hard_Tick_Relapsing_Fever_Caused_by_Borrelia.22.aspx	PCR, seroconversion
6.	Molloy PJ, Telford SR, Chowdri HR, Lepore TJ, Gugliotta JL, Weeks KE, et al. **Borrelia miyamotoi disease in the northeastern United States a case series**. Annals of Internal Medicine 2015;163(2):91-8. http://annals.org/aim/fullarticle/2301402/borrelia-miyamotoi-disease-northeastern-united-states-case-series	PCR, serology
7.	Sato K, Takano A, Konnai S, Nakao M, Ito T, Koyama K, et al. **Human infections with Borrelia miyamotoi, Japan**. Emerging Infectious Diseases 2014;20(8):1391-3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4111186/	PCR, seroconversion
8.	Hovius JWR, De Wever B, Sohne M, Brouwer MC, Coumou J, Wagemakers A, et al. **A case of meningoencephalitis by the relapsing fever spirochaete Borrelia miyamotoi in Europe**. The Lancet 2013;382(9892):658. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3987849/	Not reported in abstract/abstract not available
9.	Gugliotta JL, Goethert HK, Berardi VP, Telford ISR. **Meningoencephalitis from Borrelia miyamotoi in an immunocompromised patient**. New England Journal of Medicine 2013;368(3):240-5. https://www.nejm.org/doi/full/10.1056/NEJMoa1209039	Microscopy and a polymerase-chain-reaction (PCR) assay
10.	Chowdri HR, Gugliotta JL, Berardi VP, Goethert HK, Molloy PJ, Sterling SL, et al. **Borrelia miyamotoi Infection Presenting as Human Granulocytic Anaplasmosis A Case Report**. Annals of Internal Medicine 2013;159(1):21-+. http://annals.org/aim/fullarticle/1700642/borrelia-miyamotoi-infection-presenting-human-granulocytic-anaplasmosis-case-report	PCR
11.	Platonov AE, Karan LS, Kolyasnikova NM, Makhneva NA, Toporkova MG, Maleev VV, et al. **Humans Infected with Relapsing Fever Spirochete Borrelia miyamotoi, Russia**. Emerging Infectious Diseases 2011;17(10):1816-23. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3310649/	Not reported in abstract/abstract not available

8 Tularemia (Francisella tularensis)

We found 23 diagnostic studies and 21 case studies/case series on tularemia (Francisella tularensis).

8.1 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Yanes H, Hennebique A, Pelloux I, Boisset S, Bicout DJ, Caspar Y, et al. **Evaluation of in-house and commercial serological tests for diagnosis of human tularemia**. Journal of Clinical Microbiology 2018;56(1):e01440. http://jcm.asm.org/content/56/1/e01440-17.long	ELISA VIRapid tularemia immunochromatographic test compared to the in-house microagglutination test IFA
2.	Cubero A, Durantez C, Almaraz A, Fernandez-Lago L, Gutierrez MP, Castro MJ, et al. **Usefulness of a single-assay chemiluminescence test (Tularaemia VIRCLIA IgG + IgM monotest) for the diagnosis of human tularemia. Comparison of five serological tests**. Eur J Clin Microbiol Infect Dis 2018;37(4):643-649. https://link.springer.com/article/10.1007%2Fs10096-017-3155-9	Single-assay chemiluminescence test vs. "in-house" microagglutination test , immunochromatographic test , and "in-house" ELISA IgG, and ELISA IgM
3.	Banada PP, Deshpande S, Chakravorty S, Russo R, Occi J, Meister G, et al. **Sensitive Detection of Francisella tularensis Directly from Whole Blood by Use of the GeneXpert System**. Journal of Clinical Microbiology 2017;55(1):291-301. http://jcm.asm.org/content/55/1/291.full	Assay detection vs conventional quantitative PCR (qPCR) assay and blood culture
4.	Eremkin AV, Elagin GD, Petchenkin DV, Fomenkov OO, Bogatcheva NV, Kitmanov AA, et al. **[the Development of Immune Enzyme and Immune Chromatographic Monoclonal Test-System for Detecting Tularemia Agent]**. Klinicheskaia Laboratornaia Diagnostika 2016;61(3):184-187. https://www.ncbi.nlm.nih.gov/pubmed/27506111	Immune enzyme and immunochromatographic test

5.	Zasada AA, Forminska K, Zacharczuk K, Jacob D, Grunow R. **Comparison of eleven commercially available rapid tests for detection of Bacillus anthracis, Francisella tularensis and Yersinia pestis**. Letters in Applied Microbiology 2015;60(5):409-413. https://onlinelibrary.wiley.com/doi/abs/10.1111/lam.12392	11 commercially available rapid test kits, (abstract mentions "rapid and easy-to-perform lateral flow assays", "immunofiltration assays")
6.	Seo SH, Lee YR, Ho Jeon J, Hwang YR, Park PG, Ahn DR, et al. **Highly sensitive detection of a bio-threat pathogen by gold nanoparticle-based oligonucleotide-linked immunosorbent assay**. Biosensors & Bioelectronics 2015;64:69-73. https://www.sciencedirect.com/science/article/pii/S0956566314006265?via%3Dihub	Gold nanoparticle-based oligonucleotide-linked immunosorbent assay vs ELISA
7.	Rastawicki W, Rokosz-Chudziak N, Chrost A, Gierczynski R. **Development and evaluation of a latex agglutination test for the rapid serodiagnosis of tularemia**. Journal of Microbiological Methods 2015;112:1-2. https://www.sciencedirect.com/science/article/pii/S0167701215000664?via%3Dihub	Latex agglutination test (LAT) vs. tube agglutination test and ELISAs
8.	Chaignat V, Djordjevic-Spasic M, Ruettger A, Otto P, Klimpel D, Muller W, et al. **Performance of seven serological assays for diagnosing tularemia**. BMC Infectious Diseases 2014;14(1):234. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4021340/	ELISA, microarray, Western Blot (WB) assay
9.	Celebi B, Kilic S, Yesilyurt M, Acar B. **[Evaluation of a newly-developed ready-to-use commercial PCR kit for the molecular diagnosis of Francisella tularensis]**. Mikrobiyoloji Bulteni 2014;48(1):135-142. http://www.mikrobiyolbul.org/abstracttext.aspx?issue_id=191&ref_ind_id=21325	PCR
10.	Sharma N, Hotta A, Yamamoto Y, Fujita O, Uda A, Morikawa S, et al. **Detection of Francisella tularensis-specific antibodies in patients with tularemia by a novel competitive enzyme-linked immunosorbent assay**. Clinical & Vaccine Immunology: CVI 2013;20(1):9-16. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3535769/	ELISA andmicroagglutination test (MA)
11.	Rastawicki W, Wolaniuk N. **[Comparison of usefulness of commercial ELISA Virion/Serion, homemade ELISA and tube agglutination test in serodiagnosis of tularemia]**. **Polish.** Med Dosw Mikrobiol 2013;65(4):255-261.	ELISA and tube agglutination test

12.	Seiner DR, Colburn HA, Baird C, Bartholomew RA, Straub T, Victry K, et al. **Evaluation of the FilmArray system for detection of Bacillus anthracis, Francisella tularensis and Yersinia pestis**. J Appl Microbiol 2013;114(4):992-1000. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3617465/	PCR
13.	Kilic S, Celebi B, Yesilyurt M. **Evaluation of a commercial immunochromatographic assay for the serologic diagnosis of tularemia**. Diagnostic Microbiology & Infectious Disease 2012;74(1):1-5. https://linkinghub.elsevier.com/retrieve/pii/S0732-8893(12)00220-9	Microagglutination test
14.	Janse I, Bok JM, Hamidjaja RA, Hodemaekers HM, van Rotterdam BJ. **Development and comparison of two assay formats for parallel detection of four biothreat pathogens by using suspension microarrays**. PLoS ONE [Electronic Resource] 2012;7(2):e31958. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3280232/	PCR
15.	Buzard GS, Baker D, Wolcott MJ, Norwood DA, Dauphin LA. **Multi-platform comparison of ten commercial master mixes for probe-based real-time polymerase chain reaction detection of bioterrorism threat agents for surge preparedness**. Forensic Sci Int 2012;223(1-3):292-297. https://linkinghub.elsevier.com/retrieve/pii/S0379-0738(12)00457-4	PCR
16.	Dauphin LA, Walker RE, Petersen JM, Bowen MD. **Comparative evaluation of automated and manual commercial DNA extraction methods for detection of Francisella tularensis DNA from suspensions and spiked swabs by real-time polymerase chain reaction**. Diagnostic Microbiology & Infectious Disease 2011;70(3):299-306. https://linkinghub.elsevier.com/retrieve/pii/S0732-8893(11)00088-5	PCR
17.	Matero P, Hemmila H, Tomaso H, Piiparinen H, Rantakokko-Jalava K, Nuotio L, et al. **Rapid field detection assays for Bacillus anthracis, Brucella spp., Francisella tularensis and Yersinia pestis**. Clinical Microbiology and Infection 2011;17(1):34-43. https://linkinghub.elsevier.com/retrieve/pii/S1198-743X(14)60910-1	PCR
18.	Janse I, Hamidjaja RA, Bok JM, van Rotterdam BJ. **Reliable detection of Bacillus anthracis, Francisella tularensis and Yersinia pestis by using multiplex qPCR including internal controls for nucleic acid extraction and amplification**. BMC Microbiology 2010;10:314. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3016324/	Multiplex qPCR

19.	Splettstoesser W, Guglielmo-Viret V, Seibold E, Thullier P. **Evaluation of an immunochromatographic test for rapid and reliable serodiagnosis of human tularemia and detection of Francisella tularensis-specific antibodies in sera from different mammalian species**. Journal of Clinical Microbiology 2010;48(5):1629-1634. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2863864/	A novel immunochromatographic test (ICT) vs microagglutination
20.	Mitchell JL, Chatwell N, Christensen D, Diaper H, Minogue TD, Parsons TM, et al. **Development of real-time PCR assays for the specific detection of Francisella tularensis ssp. tularensis, holarctica and mediaasiatica**. Molecular & Cellular Probes 2010;24(2):72-76. https://www.sciencedirect.com/science/article/pii/S089085080900067X?via%3Dihub	Two real-time PCRs
21.	Molins CR, Carlson JK, Coombs J, Petersen JM. **Identification of Francisella tularensis subsp. tularensis A1 and A2 infections by real-time polymerase chain reaction**. Diagnostic Microbiology & Infectious Disease 2009;64(1):6-12. https://www.dmidjournal.com/article/S0732-8893(09)00010-8/fulltext	TaqMan PCR assays
22.	Gouriet F, Levy PY, Samson L, Drancourt M, Raoult D. **Comparison of the new InoDiag automated fluorescence multiplexed antigen microarray to the reference technique in the serodiagnosis of atypical bacterial pneumonia**. Clinical Microbiology and Infection 2008;14(12):1119-1127. https://linkinghub.elsevier.com/retrieve/pii/S1198-743X(14)61266-0	Automatic immunofluorescence assay vs. established reference techniques
23.	Jiang J, Parker CE, Fuller JR, Kawula TH, Borchers CH. **An immunoaffinity tandem mass spectrometry (iMALDI) assay for detection of Francisella tularensis**. Anal Chim Acta 2007;605(1):70-79. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2135554/	Immunoaffinity Tandem Mass Spectrometry (iMALDI) assay

8.2 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Alias T, Fallahzadeh MK, Berhe M. **Tularemia presenting as pulmonary nodules in an immunocompromised patient**. Baylor University Medical Center Proceedings 2017;30(2):175-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5349818/	Cultivation

2.	Aktepe E, Sonmezer MC, Yarimoglu S, Erdinc FS, Ertem G, Tulek N. **Delayed diagnosis of ulceroglandular tularemia: A case report. Turkish**. Klimik Dergisi 2017;30(2):83-6. https://www.researchgate.net/publication/319217722_Delayed_Diagnosis_of_Ulceroglandular_Tularemia_A_Case_Report	Microagglutination test
3.	Rojko T, Korva M, Lotric-Furlan S, Strle F, Avsic-Zupanc T. **Cluster of ulceroglandular tularemia cases in Slovenia**. Ticks and Tick-borne Diseases 2016;7(6):1193-7. https://www.sciencedirect.com/science/article/pii/S1877959X16301212?via%3Dihub	Not reported in abstract/abstract not available
4.	Longo MV, Jaton K, Pilo P, Chabanel D, Erard V. **Long-Lasting Fever and Lymphadenitis: Think about F. tularensis**. Case Reports in Medicine 2015;2015:191406. https://www.hindawi.com/journals/crim/2015/191406/	Not reported in abstract/abstract not available
5.	Forminska K, Zasada AA, Rastawicki W, Smietanska K, Bander D, Wawrzynowicz-Syczewska M, et al. **Increasing role of arthropod bites in tularaemia transmission in Poland - case reports and diagnostic methods**. Annals of Agricultural and Environmental Medicine 2015;22(3):443-6. http://www.aaem.pl/Increasing-role-of-arthropod-bites-in-tularaemia-transmission-in-Poland-case-reports,72306,0,2.html	PCR
6.	Boone I, Hassler D, Nguyen T, Splettstoesser WD, Wagner-Wiening C, Pfaff G. **Tularaemia in southwest Germany: Three cases of tick-borne transmission**. Ticks & tick-borne Diseases 2015;6(5):611-4. https://www.sciencedirect.com/science/article/pii/S1877959X15000862?via%3Dihub	Not reported in abstract/abstract not available
7.	Atchley WT, Mudrappa M, Coulter K, Bradsher RW, Johnson LG. **Bush-hogging in arkansas: A case of pulmonary tularemia from occupational exposure**. American Journal of Respiratory and Critical Care Medicine Conference: American Thoracic Society International Conference, ATS 2015;191(MeetingAbstracts). https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2015.191.1_MeetingAbstracts.A1825	Serology
8.	Sobolewska-Pilarczyk M, Pawlowska M, Halota W. **Ulceroglandular tularemia complicated by pneumonia--a case report**. Przeglad Epidemiologiczny 2014;68(3):421-4, 531. https://www.ncbi.nlm.nih.gov/pubmed/25391005	Not reported in abstract/abstract not available
9.	Celeb S, Koyuncu E, Elmas Bozdemir S, Sirvan Cetin B, Kemal Hacimustafaoglu M. **Tularemia in children: Evaluation of clinical, laboratory and treatment outcomes of 15 tularemia cases**. Guncel Pediatri 2013;11(2):57-62. https://journals.indexcopernicus.com/search/article?articleId=305983	Microagglutination test (MAT)

10.	Kader C, Balci M, Okur A, Yilmaz N, Erbay A. **Ulceroglandular tularemia: A case report**. Klimik Dergisi 2012;25(1):31-4. http://www.klimikdergisi.org/eng/ozet/9/1/Abstract	Microagglutination test
11.	Hu R. **Separating the chaff from the grain (Tularemia)**. European Review for Medical and Pharmacological Sciences 2012;16(4):554-8. https://www.ncbi.nlm.nih.gov/pubmed/22696886	Not reported in abstract/abstract not available
12.	Yesilyurt M, Kilic S, Cagasar O, Celebi B, Gul S. **Two cases of tick-borne tularemia in Yozgat province, Turkey**. Mikrobiyoloji Bulteni 2011;45(4):746-54. https://www.ncbi.nlm.nih.gov/pubmed/22090307	Seroconversion with microagglutination test and PCR
13.	Snowden J, Stovall S. **Tularemia: Retrospective Review of 10 Years' Experience in Arkansas**. Clinical Pediatrics 2011;50(1):64-8. https://journals.sagepub.com/doi/abs/10.1177/0009922810381425	Serology
14.	Moniuszko A, Zajkowska J, Pancewicz S, Kondrusik M, Grygorczuk S, Czupryna P. **Arthropod-borne tularemia in Poland: A case report**. Vector-Borne and Zoonotic Diseases 2011;11(10):1399-401. https://www.liebertpub.com/doi/full/10.1089/vbz.2010.0227?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Across-ref.org&rfr_dat=cr_pub%3Dpubmed&	Not reported in abstract/abstract not available
15.	Edouard S, Gonin K, Turc Y, Angelakis E, Socolovschi C, Raoult D. **Eschar and neck lymphadenopathy caused by Francisella tularensis after a tick bite: a case report**. Journal of Medical Case Reports [Electronic Resource] 2011;5:108. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3069950/	Serology and PCR of a biopsy from the eschar
16.	Edfors R, Smith B, Lillebaek T. **A case of tularemia in a Danish hunter. Danish**. Ugeskrift for laeger 2010;172(5):381-2. https://www.ncbi.nlm.nih.gov/pubmed/20122335	Not reported in abstract/abstract not available
17.	Switaj K, Olszynska-Krowicka M, Zarnowska-Prymek H, Zaborowski P. **Tularaemia after tick exposure - Typical presentation of rare disease misdiagnosed as atypical presentation of common diseases: A case report**. Cases Journal 2009;2 (7) (no pagination)(7954). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2740238/	Serology
18.	Stoecker WV, Calcara DA, Malters JM, Clonts M, Everett ED. **Tick-borne febrile illnesses lacking specific symptoms**. Missouri Medicine 2009;106(4):304-8.	Serology

	https://www.ncbi.nlm.nih.gov/pubmed/19753926	
19.	Lubbert C, Taege C, Seufferlein T, Grunow R. **Prolonged course of tick-borne ulceroglandular tularemia in a 20-year-old patient in Germany--case report and review of the literature. German**. Deutsche medizinische Wochenschrift 2009;134(27):1405-10. https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0029-1225296	Serology and retrospective real-time PCR
20.	Limper M, Roest HI, van Gorp EC. **A patient with a fever and an eschar caused by tularemia. Dutch**. Nederlands tijdschrift voor geneeskunde 2009;153:B84. https://www.ncbi.nlm.nih.gov/pubmed/19818182	Serology
21.	Konstantinou MP, Abecassis-Cotta S, Valeyrie-Allanore L, Ortonne N, Maurin M, Roujeau JC, et al. **Severe tularaemia mimicking glandular tuberculosis during adalimumab therapy**. Annales De Dermatologie Et De Venereologie 2009;136(10):718-22. https://www.em-consulte.com/article/227108/alertePM	Serology and PCR

9 Cat scratch disease (Bartonella spp)

We found one systematic review, 24 diagnostic studies and 125 case studies/case series on cat scratch disease (Bartonella).

9.1 Systematic reviews

	Reference	Diagnostic test(s) studied
1.	Sanchez Clemente N, Ugarte-Gil CA, Solorzano N, Maguina C, Pachas P, Blazes D, et al. **Bartonella bacilliformis: a systematic review of the literature to guide the research agenda for elimination**. PLoS Neglected Tropical Diseases [electronic re-source] 2012;6(10):e1819. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3493376/	Different tests studied

9.2 Diagnostic studies

	Reference	Diagnostic test(s) studied
1.	Tsuneoka H, Yanagihara M, Tanimoto A, Tokuda N, Otsuyama KI, Nojima J, et al. **The utility of a country-specific Bartonella henselae antigen in an IgM-indirect fluorescent antibody assay for the improved diagnosis of cat scratch disease**. Diagnostic Microbiology and Infectious Disease 2017;87(1):22-24. https://www.dmidjournal.com/article/S0732-8893(16)30339-X/fulltext	IFA
2.	Liu YY, Zhao LS, Song XP, Du PC, Li DM, Chen ZK, et al. **Development of fluorogenic probe-based and high-resolution melting-based polymerase chain reaction assays for the detection and differentiation of Bartonella quintana and Bartonella henselae**. Journal of Microbiological Methods 2017;138:30-36. https://www.sciencedirect.com/science/article/pii/S0167701216301439?via%3Dihub	PCR
3.	Parra E, Segura F, Tijero J, Pons I, Nogueras MM. **Development of a real-time PCR for Bartonella spp. detection, a current emerging microorganism**. Molecular & Cellular Probes 2017;32:55-59. https://linkinghub.elsevier.com/retrieve/pii/S0890-8508(16)30082-2	Real-time PCR assay using SYBR Green
4.	Liu J, Ochieng C, Wiersma S, Stroher U, Towner JS, Whitmer S, et al. **Development of a TaqMan Array Card for Acute-Febrile-Illness Outbreak Investigation and Surveillance of Emerging Pathogens, Including Ebola Virus**. Journal of Clinical Microbiology 2016;54(1):49-58. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4702733/	Real-time PCR-based TaqMan array card (TAC)
5.	Otsuyama KI, Tsuneoka H, Kondou K, Yanagihara M, Tokuda N, Shirasawa B, et al. **Development of a highly specific IgM enzyme-linked immunosorbent assay for bartonella henselae using refined N-lauroyl-sarcosine-insoluble proteins for serodiagnosis of cat scratch disease**. Journal of Clinical Microbiology 2016;54(4):1058-1064. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4809944/	ELISAs vs IgM indirect fluorescent antibody assay.

6.	El-Kholy AA, El-Rachidi NG, El-Enany MG, AbdulRahman EM, Mohamed RM, Rizk HH. **Impact of serology and molecular methods on improving the microbiologic diagnosis of infective endocarditis in Egypt**. Infection 2015;43(5):523-529. https://link.springer.com/article/10.1007%2Fs15010-015-0761-2	Serology and PCR
7.	Ferrara F, Di Niro R, D'Angelo S, Busetti M, Marzari R, Not T, et al. **Development of an enzyme-linked immunosorbent assay for Bartonella henselae infection detection**. Letters in Applied Microbiology 2014;59(3):253-262. https://onlinelibrary.wiley.com/doi/abs/10.1111/lam.12286	ELISA
8.	Angkasekwinai N, Atkins EH, Romero S, Grieco J, Chao CC, Ching WM. **An evaluation study of enzyme-linked immunosorbent assay (ELISA) using recombinant protein Pap31 for detection of antibody against Bartonella bacilliformis infection among the Peruvian population**. American Journal of Tropical Medicine & Hygiene 2014;90(4):690-696. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3973514/	ELISA vs. IFA
9.	Kawasato KH, de Oliveira LC, Velho PE, Yamamoto L, Del Negro GM, Okay TS. **Detection of Bartonella henselae DNA in clinical samples including peripheral blood of immune competent and immune compromised patients by three nested amplifications**. Revista do Instituto de Medicina Tropical de Sao Paulo 2013;55(1):1-6. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0036-46652013000100001	PCR
10.	Diddi K, Chaudhry R, Sharma N, Dhawan B. **Strategy for identification & characterization of Bartonella henselae with conventional & molecular methods**. Indian Journal of Medical Research 2013;137(2):380-387. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3657863/	PCR and restriction fragment length polymorphism
11.	Smit P, Peeling R, Garcia P, Torres L, Perez-Lu J, Moore D, et al. **Short report: dried blood spots for qPCR diagnosis of acute Bartonella bacilliformis infection**. American journal of tropical medicine and hygiene 2013;89(5):988-990. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3820349/	rt-PCR
12.	Pultorak EL, Maggi RG, Mascarelli PE, Breitschwerdt EB. **Serial testing from a 3-day collection period by use of the Bartonella Alphaproteobacteria growth medium platform may enhance the sensitivity of Bartonella species detection in bacteremic human patients**. Journal of Clinical Microbiology 2013;51(6):1673-1677. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3716093/	PCR

13.	Bergmans AM, Rossen JW. **Detection of Bartonella spp. DNA in clinical specimens using an internally controlled real-time PCR assay**. Methods in Molecular Biology 2013;943:217-228. https://link.springer.com/protocol/10.1007%2F978-1-60327-353-4_14	Real-time PCR
14.	Abarca K, Winter M, Marsac D, Palma C, Contreras AM, Ferres M. **Accuracy and diagnostic utility of IgM in Bartonella henselae infections. [Spanish]**. Revista chilena de infectologia : organo oficial de la Sociedad Chilena de Infectologia 2013;30(2):125-128. https://scielo.conicyt.cl/scielo.php?script=sci_arttext&pid=S0716-10182013000200001&lng=en&nrm=iso&tlng=en	IFA
15.	Tsuruoka K, Tsuneoka H, Kawano M, Yanagihara M, Nojima J, Tanaka T, et al. **Evaluation of IgG ELISA using N-lauroyl-sarcosine-soluble proteins of Bartonella henselae for highly specific serodiagnosis of cat scratch disease**. Diagnostic Microbiology and Infectious Disease 2012;74(3):230-235. https://linkinghub.elsevier.com/retrieve/pii/S0732-8893(12)00279-9	ELISA
16.	Maggi RG, Mascarelli PE, Pultorak EL, Hegarty BC, Bradley JM, Mozayeni BR, et al. **Bartonella spp. bacteremia in high-risk immunocompetent patients**. Diagnostic Microbiology & Infectious Disease 2011;71(4):430-437. https://www.dmidjournal.com/article/S0732-8893(11)00355-5/fulltext	PCR and serology
17.	Saisongkorh W, Kowalczewska M, Azza S, Decloquement P, Rolain JM, Raoult D. **Identification of candidate proteins for the diagnosis of Bartonella henselae infections using an immunoproteomic approach**. FEMS Microbiology Letters 2010;310(2):158-167. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1574-6968.2010.02058.x	Serology and identification of protein markers
18.	Vermeulen MJ, Verbakel H, Notermans DW, Reimerink JH, Peeters MF. **Evaluation of sensitivity, specificity and cross-reactivity in Bartonella henselae serology**. Journal of Medical Microbiology 2010;59(Pt 6):743-745. Record no: 1620 http://jmm.microbiologyresearch.org/content/journal/jmm/10.1099/jmm.0.015248-0#tab2	Serology and PCR
19.	Caponetti GC, Pantanowitz L, Marconi S, Havens JM, Lamps LW, Otis CN. **Evaluation of immunohistochemistry in identifying bartonella henselae in cat-scratch disease**. American Journal of Clinical Pathology 2009;131(2):250-256. https://academic.oup.com/ajcp/article/131/2/250/1766127	Serology and pCR

20.	Tang YW. **Duplex PCR assay simultaneously detecting and differentiating Bartonella quintana, B. henselae, and Coxiella burnetii in surgical heart valve specimens**. Journal of Clinical Microbiology 2009;47(8):2647-2650. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725655/	PCR
21.	Hoey JG, Valois-Cruz F, Goldenberg H, Voskoboynik Y, Pfiffner J, Tilton RC, et al. **Development of an immunoglobulin M capture-based enzyme-linked immunosorbent assay for diagnosis of acute infections with Bartonella henselae**. Clinical & Vaccine Immunology: CVI 2009;16(2):282-284. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2643531/	ELISA
22.	Fournier PE, Couderc C, Buffet S, Flaudrops C, Raoult D. **Rapid and cost-effective identification of Bartonella species using mass spectrometry**. Journal of Medical Microbiology 2009;58(Pt 9):1154-1159. http://jmm.microbiologyresearch.org/content/journal/jmm/10.1099/jmm.0.009647-0#tab2	MALDI-TOF MS
23.	Wagner CL, Riess T, Linke D, Eberhardt C, Schafer A, Reutter S, et al. **Use of Bartonella adhesin A (BadA) immunoblotting in the serodiagnosis of Bartonella henselae infections**. Ijmm International Journal of Medical Microbiology 2008;298(7-8):579-590. https://www.sciencedirect.com/science/article/pii/S1438422108000325	IFA and immunoblotting
24.	Vermeulen MJ, Herremans M, Verbakel H, Bergmans AM, Roord JJ, van Dijken PJ, et al. **Serological testing for Bartonella henselae infections in The Netherlands: clinical evaluation of immunofluorescence assay and ELISA**. Clinical Microbiology & Infection 2007;13(6):627-634. https://linkinghub.elsevier.com/retrieve/pii/S1198-743X(14)62230-8	IFA and ELISA

9.3 Case studies or case series

	Reference	Diagnostic test(s) studied
1.	Sendi P, Hirzel C, Bloch A, Fischer U, Jeannet N, Berlinger L, et al. **Bartonella-associated transverse myelitis**. Emerging Infectious Diseases 2017;23(4):712-3. https://wwwnc.cdc.gov/eid/article/23/4/16-1733_article	Not reported in abstract/abstract not available

2.	Kaufman DL, Kogelnik AM, Mozayeni RB, Cherry NA, Breitschwerdt EB. **Neurological and immunological dysfunction in two patients with Bartonella henselae bacteremia**. Clinical Case Reports 2017;5(6):931-5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5458018/	Not reported in abstract/abstract not available
3.	Zepeda TJ, Morales SJ, Letelier AH, Delpiano ML. **Osteomielitis vertebral por Bartonella henselae: A proposito de un caso. Spanish**. Revista Chilena de Pediatria 2016;87(1):53-8. https://scielo.conicyt.cl/scielo.php?script=sci_abstract&pid=S0370-41062016000100010&lng=en&nrm=iso&tlng=en	Serology
4.	Welschen DVDV. **Neurorretinitis by Bartonella henselae: a case report and review of the literature**. Revista Mexicana de Oftalmologia 2016;90(5):235-41. https://www.sciencedirect.com/science/article/pii/S0187451915001079	Not reported in abstract/abstract not available
5.	Weilg C, Del Aguila O, Mazulis F, Silva-Caso W, Alva-Urcia C, Cerpa-Polar R, et al. **Seronegative disseminated Bartonella spp. infection in an immunocompromised patient**. Asian Pacific Journal of Tropical Medicine 2016;9(12):1222-5. https://www.sciencedirect.com/science/article/pii/S1995764516304552	PCR and serology
6.	Verdier-Watts F, Peloni JM, Piegay F, Gerome P, Aussoleil A, Durand-de-Gevigney G, et al. **An exceptional case of tricuspid infective endocarditis due to Bartonella henseale revealed by an old pulmonary embolism**. Annales de Cardiologie et d Angeiologie 2016;65(1):48-50. https://www.sciencedirect.com/science/article/pii/S0003392815000062?via%3Dihub	Serology and PCR
7.	Sosa T, Goldstein B, Cnota J, Bryant R, Frenck R, Washam M, et al. **Melody valve bartonella henselae endocarditis in an afebrile teen: A case report**. Pediatrics 2016;137(1):e20151548. http://pediatrics.aappublications.org/content/137/1/e20151548.long	Serology
8.	Saison J, Harbaoui B, Bouchiat C, Pozzi M, Ferry T. **Unexpected severe native aortic subacute endocarditis due to Bartonella quintana in a 40-year-old woman with good socioeconomic condition**. BMJ Case Reports 2016;20:20. https://casereports.bmj.com/content/2016/bcr-2016-216355.full	Serololgy
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91.	Celebi B, Yalcin E, Babur C. **Fever of unknown origin and detection of Bartonella henselae IgG seropositivity: a case report**. Mikrobiyoloji Bulteni 2010;44(3):489-94. https://www.ncbi.nlm.nih.gov/pubmed/21064000	IFA
92.	Breitschwerdt EB, Maggi RG, Lantos PM, Woods CW, Hegarty BC, Bradley JM. **Bartonella vinsonii subsp berkhoffii and Bartonella henselae bacteremia in a father and daughter with neurological disease**. Parasites & Vectors 2010;3:9. https://parasitesandvectors.biomedcentral.com/articles/10.1186/1756-3305-3-29	PCR and IFA.
93.	Bolton JG, Galeckas KJ, Satter EK. **Inoculation bartonellosis in an adult: a case report**. Cutis 2010;85(1):37-42. https://www.ncbi.nlm.nih.gov/pubmed/20184210	Not reported in abstract/abstract not available
94.	Bernabeu-Wittel J, Luque R, Corbi R, Mantrana-Bermejo M, Navarrete M, Vallejo A, et al. **Bacillary angiomatosis with atypical clinical presentation in an immunocompetent patient**. Indian Journal of Dermatology, Venereology & Leprology 2010;76(6):682-5.	PCR

	http://www.ijdvl.com/article.asp?issn=0378-6323;year=2010;volume=76;issue=6;spage=682;epage=685;aulast=Berna-beu%2DWittel	
95.	Baty G, Lanotte P, Hocqueloux L, Prazuck T, Bret L, Romano M, et al. **PCR rDNA 16S used for the etiological diagnosis of blood culture negative endocarditis**. Medecine et Maladies Infectieuses 2010;40(6):358-62. https://www.sciencedirect.com/science/article/pii/S0399077X09002224?via%3Dihub	16S rDNA PCR, followed by sequencing
96.	Angelakis E, Pulcini C, Waton J, Imbert P, Socolovschi C, Edouard S, et al. **Scalp eschar and neck lymphadenopathy caused by Bartonella henselae after Tick Bite**. Clinical Infectious Diseases 2010;50(4):549-51. https://academic.oup.com/cid/article/50/4/549/352847	Not reported in abstract/abstract not available
97.	Vitale G, Incandela S, Incandela C, Micalizzi A, Mansueto P. **Isolation and characterization of Bartonella quintana from the parotid gland of an immunocompetent man**. Journal of Clinical Microbiology 2009;47(3):862-4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2650900/	"High titers of immunoglobulin G (IgG) and IgM antibodies and of culture isolation of a causative agent from parotid aspirate"
98.	Sugiyama H, Sahara M, Imai Y, Ono M, Okamoto K, Kikuchi K, et al. **Infective endocarditis by Bartonella quintana masquerading as antineutrophil cytoplasmic antibody-associated small vessel vasculitis**. Cardiology 2009;114(3):208-11. https://www.karger.com/Article/Abstract/228645	Serology, PCR
99.	Mastrandrea S, Simonetta Taras M, Capitta P, Tola S, Marras V, Strusi G, et al. **Detection of Bartonella henselae - DNA in macronodular hepatic lesions of an immunocompetent woman**. Clinical Microbiology and Infection 2009;15(SUPPL. 2):116-7. https://linkinghub.elsevier.com/retrieve/pii/S1198-743X(14)63506-0	Not reported in abstract/abstract not available
100.	Martin L, Vidal L, Campins A, Salva F, Riera M, Carrillo A, et al. **Bartonella as a cause of blood culture-negative endocarditis. Description of five cases**. Revista Espanola de Cardiologia 2009;62(6):694-7. http://www.revespcardiol.org/en/ibartonella-i-as-cause-of-blood/articulo/13139389/	Serology, PCR
101.	Magalhaes RF, Urso Pitassi LH, Lania BG, Barjas-Castro ML, Neves Ferreira Velho PE. **Bartonellosis as cause of death after red blood cell unit transfusion**. Ultrastructural Pathology 2009;33(4):151-4. https://www.tandfonline.com/doi/abs/10.3109/01913120902785567?journalCode=iusp20	Not reported in abstract/abstract not available
102.	Lienhardt B, Irani S, Gaspert A, Weishaupt D, Boehler A. **Disseminated infection with Bartonella henselae in a lung transplant recipient**. Journal of Heart & Lung Transplantation 2009;28(7):736-9.	Not reported in abstract/abstract not available

	https://www.jhltonline.org/article/S1053-2498(09)00189-2/abstract	
103.	Lange D, Oeder C, Waltermann K, Mueller A, Oehme A, Rohrberg R, et al. **Bacillary angiomatosis**. Journal der Deutschen Dermatologischen Gesellschaft 2009;7(9):767-9. https://onlinelibrary.wiley.com/doi/full/10.1111/j.1610-0387.2009.07055.x	Histology and PCR
104.	Irshad FA, Gordon RA. **Bartonella henselae neuroretinitis in a 15-year-old girl with chronic myelogenous leukemia**. Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus 2009;13(6):602-4. https://www.jaapos.org/article/S1091-8531(09)00311-5/abstract	Serology
105.	Hernandez-Da Mota SE, Escalante-Razo FA. **Bartonellosis causing bilateral Leber neuroretinitis: A case report**. European Journal of Ophthalmology 2009;19(2):307-9. https://www.ncbi.nlm.nih.gov/pubmed/19253255	Not reported in abstract/abstract not available
106.	de La Blanchardiere A, Fournier PE, Haustraete E, du Cheyron D, Lepage O, Verdon R. **Infective endocarditis due to Bartonella henselae following a rupture of a cerebral aneurysm**. Medecine et Maladies Infectieuses 2009;39(6):394-6. https://www.sciencedirect.com/science/article/pii/S0399077X08004277?via%3Dihub	Serology, PCR
107.	Das BB, Wasser E, Bryant KA, Woods CR, Yang SG, Zahn M. **Culture negative endocarditis caused by Bartonella henselae in a child with congenital heart disease**. Pediatric Infectious Disease Journal 2009;28(10):922-5. https://insights.ovid.com/pubmed?pmid=19738506	Serology, PCR
108.	Yerebakan C, Westphal B, Aepinus C. **Infective endocarditis due to Bartonella quintana: a challenging diagnostic entity**. Acta Cardiologica 2008;63(4):519-21. http://poj.peeters-leuven.be/content.php?url=article&id=2033053&journal_code=AC	Not reported in abstract/abstract not available
109.	Tager FM, Jahnsen KJ, Mediavilla RM, Burgos LR. **Ocular bartonellosis: Report of three clinical cases. Spanish**. Revista Chilena de Infectologia 2008;25(1):58-63. https://scielo.conicyt.cl/scielo.php?script=sci_arttext&pid=S0716-10182008000100012&lng=en&nrm=iso&tlng=en	Not reported in abstract/abstract not available
110.	Scolfaro C, Mignone F, Gennari F, Alfarano A, Veltri A, Romagnoli R, et al. **Possible donor-recipient bartonellosis transmission in a pediatric liver transplant**. Transplant Infectious Disease 2008;10(6):431-3. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1399-3062.2008.00326.x	Not reported in abstract/abstract not available

111.	Merle De Boever C, Mura F, Brun M, Reynes J. **Ocular bartonellosis in an HIV-HVC coinfected patient**. Medecine et Maladies Infectieuses 2008;38(9):504-6. https://www.sciencedirect.com/science/article/pii/S0399077X08001637?via%3Dihub	Serology
112.	Lydy SL, Eremeeva ME, Asnis D, Paddock CD, Nicholson WL, Silverman DJ, et al. **Isolation and characterization of Bartonella bacilliformis from an expatriate Ecuadorian**. Journal of Clinical Microbiology 2008;46(2):627-37. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2238110/	Immunohistochemistry, culture, multilocus sequence typing and IFA
113.	Lejko-Zupanc T, Slemenik-Pusnik C, Kozelj M, Klokocovnik T, Avsic-Zupanc T, Dolenc-Strazar Z, et al. **Native valve endocarditis due to Bartonella henselae in an immunocompetent man**. Wiener Klinische Wochenschrift 2008;120(7-8):246-9. https://link.springer.com/article/10.1007%2Fs00508-008-0951-3	Serology and PCR
114.	Gescher DM, Mallmann C, Kovacevic D, Schmiedel D, Borges AC, Schweickert B, et al. **A view on Bartonella quintana endocarditis--confirming the molecular diagnosis by specific fluorescence in situ hybridization**. Diagnostic Microbiology & Infectious Disease 2008;60(1):99-103. https://www.researchgate.net/publication/5955674_A_view_on_Bartonella_quintana_endocarditis-confirming_the_molecular_diagnosis_by_specific_fluorescence_in_situ_hybridization	PCR and oligonucleotide fluorescence in situ hybridization
115.	Donnio A, Jean-Charles A, Merle H. **Macular hole following Bartonella henselae neuroretinitis**. European Journal of Ophthalmology 2008;18(3):456-8. https://www.ncbi.nlm.nih.gov/pubmed/18465733	Not reported in abstract/abstract not available
116.	De Clerck KF, Van Offel JF, Vlieghe E, Van Marck E, Stevens WJ. **Bartonella endocarditis mimicking adult Still's disease**. Acta Clinica Belgica 2008;63(3):190-2. https://www.tandfonline.com/doi/abs/10.1179/acb.2008.030	Serology, PCR
117.	Wimmersberger Y, Baglivo E. **Bartonella henselae infection presenting as a unilateral acute maculopathy**. Klinische Monatsblatter fur Augenheilkunde 2007;224(4):311-3. https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-2007-962855	Serology
118.	Vasquez TP, Chanqueo CL, Garcia CP, Poggi MH, Ferres GM, Bustos MM, et al. **Bacillary angiomatosis caused by Bartonella quintana in an human immunodeficiency virus positive patient**. Revista Chilena de Infectologia 2007;24(2):155-9. https://scielo.conicyt.cl/scielo.php?script=sci_arttext&pid=S0716-10182007000200012&lng=en&nrm=iso&tlng=en	Serology, PCR

119.	Sedlackova L, Bartosova D, Vydrzalova P, Crhova K, Zarosska E, Holcikova A, et al. **Abscessing lymphadenitis in a 1.5-year-old boy**. Klinicka Mikrobiologie a Infekcni Lekarstvi 2007;13(3):119-21. https://www.ncbi.nlm.nih.gov/pubmed/17703405	Not reported in abstract/abstract not available
120.	Melikian AL, Mediannikov O, Kaplanskaia IB, Komarova AI, Tarasevich IV. **Bartonella infection in hematological practice**. Terapevticheskii Arkhiv 2007;79(4):58-62. https://www.ncbi.nlm.nih.gov/pubmed/17564022	Serology, PCR
121.	Lamas C, Favacho A, Ramos RG, Santos MS, Ferravoli GI, Weksler C, et al. **Bartonella native valve endocarditis: the first Brazilian case alive and well**. Brazilian Journal of Infectious Diseases 2007;11(6):591-4. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-86702007000600012&lng=en&nrm=iso&tlng=en	Serology
122.	Kodama Y, Maeno N, Nishi J, Imuta N, Oda H, Tanaka S, et al. **Multifocal osteomyelitis due to Bartonella henselae in a child without focal pain**. Journal of Infection & Chemotherapy 2007;13(5):350-2. https://linkinghub.elsevier.com/retrieve/pii/S1341-321X(07)70838-3	Magnetic resonance imaging and PCR
123.	Hoffman RM, AboulHosn J, Child JS, Pegues DA. **Bartonella endocarditis in complex congenital heart disease**. Congenital Heart Disease 2007;2(1):79-84. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1747-0803.2007.00077.x	Serology, PCR
124.	Dardenne S, Coche E, Weynand B, Poncelet A, Zech F, De Meyer M. **High suspicion of bacillary angiomatosis in a kidney transplant recipient: a difficult way to diagnose -case report**. Transplantation Proceedings 2007;39(1):311-3. https://www.sciencedirect.com/science/article/pii/S0041134506014655?via%3Dihub	Histology, PCR and immunohistochemy
125.	Borboli S, Afshari NA, Watkins L, Foster CS. **Presumed oculoglandular syndrome from Bartonella quintana**. Ocular Immunology & Inflammation 2007;15(1):41-3. https://www.tandfonline.com/doi/abs/10.1080/09273940601077157?journalCode=ioii20	Serology

Results part 2: Co-infections

The search resulted in 524 unique references. 118 references were possibly relevant according to the inclusion criteria.

Sorting categories

Because of the nature of "co-infections" where two or more infections are studied at the same time, it was not meaningful to categorize the studies based on infection type. The majority of the references referred to studies on co-infections with Lyme borreliosis (Borrelia), and we sorted these into one category. This also includes references where the main object was to study one of the other tick-borne infections, but where the authors mentioned the prevalence or identification of co-infection with borreliosis in the abstract. We then categorized the references into systematic reviews, non-systematic reviews, prevalence studies, diagnostic studies and case studies/case series.
We also categorized other studies not mentioning borreliosis according to the same study types.

Lyme borreliosis co-infections

We found four systematic reviews, eleven non-systematic reviews, 15 diagnostic studies, 50 prevalence studies and 25 case studies on Lyme borreliosis co-infections.

Systematic reviews

1. Stokes G, Blanchard L, Sutcliffe K, Dickson K, Brunton G, Burchett H, et al. **Prevalence, diagnosis, treatment and prevention of Lyme disease: an evidence map and four systematic reviews**. 2017:106-10. http://eppi.ioe.ac.uk/cms/Default.aspx?tabid=3701

2. Lantos PM, Wormser GP. **Chronic coinfections in patients diagnosed with chronic lyme disease: a systematic review**. Am J Med 2014;127(11):1105-10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4252587/

3. Borgermans L, Goderis G, Vandevoorde J, Devroey D. **Relevance of chronic lyme disease to family medicine as a complex multidimensional chronic disease construct: a systematic review**. International Journal of Family Medicine Print 2014;2014:138016. https://www.hindawi.com/journals/ijfm/2014/138016/

4. Nieto NC, Foley JE. **Meta-analysis of coinfection and coexposure with Borrelia burgdorferi and Anaplasma phagocytophilum in humans, domestic animals, wildlife, and Ixodes ricinus-complex ticks**. Vector borne zoonotic dis 2009;9(1):93-102. https://www.ncbi.nlm.nih.gov/pubmed/18789001

Review articles (non-systematic)

1. Guzman N, Beidas SO. **Anaplasma Phagocytophilum (Anaplasmosis)**. StatPearls Publishing 2018;01:01. https://www.ncbi.nlm.nih.gov/books/NBK513341/

2. Stinco G, Bergamo S. **Impact of co-infections in lyme disease**. Open Dermatology Journal 2016;10(Suppl 1: M6):55-61. https://benthamopen.com/FULLTEXT/TODJ-10-55

3. Diuk-Wasser MA, Vannier E, Krause PJ. **Coinfection by Ixodes Tick-Borne Pathogens: Ecological, Epidemiological, and Clinical Consequences**. Trends Parasitol 2016;32(1):30-42. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4713283/

4. Caulfield AJ, Pritt BS. **Lyme Disease Coinfections in the United States**. Clin Lab Med 2015;35(4):827-46. https://www.sciencedirect.com/science/article/pii/S0272271215000992?via%3Dihub

5. Bakken JS, Dumler JS. **Human granulocytic anaplasmosis**. Infect Dis Clin North Am 2015;29(2):341-55. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4441757/

6. Perronne C. **Lyme and associated tick-borne diseases: global challenges in the context of a public health threat**. Front 2014;4:74. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4042490/

7. Broker M. **Following a tick bite: double infections by tick-borne encephalitis virus and the spirochete Borrelia and other potential multiple infections**. Zoonoses Public Health 2012;59(3):176-80. https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1863-2378.2011.01435.x

8. Berghoff W. **Chronic Lyme Disease and Co-infections: Differential Diagnosis**. Open Neurol J 2012;6:158-78. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3565243/

9. Stricker RB, Johnson L. **Lyme disease: the next decade**. Infect 2011;4:1-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3108755/

10. Gern L, Lienhard R, Peter O. **Diseases and pathogenic agents transmitted by ticks in Switzerland. [French]**. Revue Medicale Suisse 2010;6(266):1906-9. https://www.ncbi.nlm.nih.gov/pubmed/21089555

11. Stricker RB. **Counterpoint: long-term antibiotic therapy improves persistent symptoms associated with lyme disease**. Clin Infect Dis 2007;45(2):149-57.
https://www.ncbi.nlm.nih.gov/pubmed/17578772

Diagnostic studies

1. Primus S, Akoolo L, Schlachter S, Gedroic K, Rojtman AD, Parveen N. **Efficient detection of symptomatic and asymptomatic patient samples for Babesia microti and Borrelia burgdorferi infection by multiplex qPCR**. PLoS ONE 2018;13(5):e0196748.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5945202/

2. Molloy PJ, Weeks KE, Todd B, Wormser GP. **Seroreactivity to the C6 Peptide in Borrelia miyamotoi Infections Occurring in the Northeastern United States**. Clin Infect Dis 2018;66(9):1407-10.
https://academic.oup.com/cid/article-abstract/66/9/1407/4631884?redirectedFrom=fulltext

3. Schlachter S, Chan K, Marras SAE, Parveen N. **Detection and Differentiation of Lyme Spirochetes and Other Tick-Borne Pathogens from Blood Using Real-Time PCR with Molecular Beacons**. Methods Mol Biol 2017;1616:155-70.
https://link.springer.com/protocol/10.1007%2F978-1-4939-7037-7_10

4. Huang NL, Ye L, Lv H, Du YX, Schneider M, Fan LB, et al. **A biochip-based combined immunoassay for detection of serological status of Borrelia burgdorferi in Lyme borreliosis**. Clin Chim Acta 2017;472:13-9.
https://www.sciencedirect.com/science/article/pii/S0009898117302504?via%3Dihub

5. Jahfari S, Sarksyan DS, Kolyasnikova NM, Hovius JW, Sprong H, Platonov AE. **Evaluation of a serological test for the diagnosis of Borrelia miyamotoi disease in Europe**. J Microbiol Methods 2017;136:11-6.
https://www.sciencedirect.com/science/article/pii/S0167701217300532?via%3Dihub

6. Tomasiewicz K, Chmielewska-Badora J, Zwolinski J, Murias-Brylowska E. **Analysis of main T-cell subsets and activated T supressor/cytotoxic cells in patients with Borrelia burgdorferi s. lato only infection and co-infections with Anaplasma phagocytophilum, Bartonella spp. and Babesia microti**. Ann Agric Environ Med 2016;23(1):111-5.

https://www.ncbi.nlm.nih.gov/pubmed/27007527

7. Minoranskaya NS, Sarap PV, Andronova NV, Minoranskaya EI. **Clinical and Laboratory Predictors for Forecasting the Outcomes of Ixodes Tick-Borne Borreliosis. [Russian]**. Vestnik Rossiiskoi akademii meditsinskikh nauk / Rossiiskaia akademiia meditsinskikh nauk 2015;(3):378-85. https://www.ncbi.nlm.nih.gov/pubmed/26495729

8. McManus M, Cincotta A. **Effects of Borrelia on host immune system: Possible consequences for diagnostics**. Advances in Integrative Medicine 2015;2(2):81-9. https://www.sciencedirect.com/science/article/pii/S2212962614000601

9. Jaaskelainen AJ, Viitala SM, Kurkela S, Hepojold S, Sillanpaa H, Kallio-Kokko H, et al. **Performance of a multiplexed serological microarray for the detection of antibodies against central nervous system pathogens**. J Microbiol Methods 2014;100:27-31. https://www.sciencedirect.com/science/article/pii/S0167701214000517?via%3Dihub

10. Chan K, Marras SA, Parveen N. **Sensitive multiplex PCR assay to differentiate Lyme spirochetes and emerging pathogens Anaplasma phagocytophilum and Babesia microti**. BMC Microbiol 2013;13:295. https://bmcmicrobiol.biomedcentral.com/articles/10.1186/1471-2180-13-295

11. Higuchi ML, Palomino SAP, Reis MM, Mangini S, Bocchi EA, Pomerantzeff PM, et al. **Simultaneous detection of multiple viruses and bacteria by both electron microscopy and immunohistochemistry techniques suggests a role for co-infection in dilated cardiomyopathy**. European Journal of Heart Failure 2013;1):S67. https://onlinelibrary.wiley.com/doi/10.1093/eurjhf/hst008

12. Mihailescu P, Cretu C. **Correlation between indirect immunofluorescence and Western blot, serological techniques used for the diagnosis of Lyme disease**. Clinical Microbiology and Infection 2012;3):592-3. https://www.sciencedirect.com/science/article/pii/S1198743X15600787?via%3Dihub

13. Schwarzova K. **Laboratory diagnostic methods in suspected disseminated lyme disease: A comparison of different techniques**. Acta Microbiologica et Immunologica Hungarica 2011;1):210-1. https://akademiai.com/doi/abs/10.1556/AMicr.58.2011.Suppl.2

14. Karan LS, Koliasnikova NM, Toporkova MG, Makhneva MA, Nadezhdina MV, Esaulkova A, et al. **[Usage of real time polymerase chain reaction for diagnostics of different tick-borne infections]**. Zh Mikrobiol Epidemiol Immunobiol 2010;(3):72-7. https://www.ncbi.nlm.nih.gov/pubmed/20734723

15. Floris R, Menardi G, Bressan R, Trevisan G, Ortenzio S, Rorai E, et al. **Evaluation of a genotyping method based on the ospA gene to detect Borrelia burgdorferi sensu lato in multiple samples of lyme borreliosis patients**. New Microbiol 2007;30(4):399-410. http://www.newmicrobiologica.org/PUB/allegati_pdf/2007/4/399.pdf

Prevalence studies

1. Sowula K, Skladzien J, Szaleniec J, Gawlik J. **Otolaryngological symptoms in patients treated for tick-borne diseases**. Otolaryngol Pol 2018;72(1):30-4. https://otolaryngologypl.com/resources/html/article/details?id=167291&language=en

2. Ocias LF, Dessau RB, Lebech AM, Jorgensen CS, Petersen RF, Krogfelt KA. **Evidence of rickettsiae in Danish patients tested for Lyme neuroborreliosis: a retrospective study of archival samples**. BMC Infect Dis 2018;18(1):325. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6042448/

3. Fesler MC, Middelveen MJ, Stricker RB. **Clinical evaluation of Morgellons disease in a cohort of North American patients**. Dermatol Reports 2018;10(1):7660. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5941186/

4. Liu HB, Wei R, Ni XB, Zheng YC, Huo QB, Jiang BG, et al. **The prevalence and clinical characteristics of tick-borne diseases at One Sentinel Hospital in Northeastern China**. Parasitology 2018:1-7. https://www.cambridge.org/core/journals/parasitology/article/prevalence-and-clinical-characteristics-of-tickborne-diseases-at-one-sentinel-hospital-in-northeastern-china/5FE0DB3BA6DBC3B9C8A5761F66961448

5. Dunaj J, Moniuszko-Malinowska A, Swiecicka I, Andersson M, Czupryna P, Rutkowski K, et al. **Tick-borne infections and co-infections in patients with non-specific symptoms in Poland**. Adv Med Sci 2018;63(1):167-72. https://www.sciencedirect.com/science/article/pii/S1896112617300652

6. Boyer PH, Kieffer P, de Martino SJ, Zilliox L, Vogel JY, Jaulhac B, et al. **Borrelia burgdorferi sl and tick-borne encephalitis virus coinfection in Eastern France**. Med Mal Infect 2018;48(3):218-20.
https://www.sciencedirect.com/science/article/pii/S0399077X1730625X?via%3Dihub

7. Moniuszko-Malinowska A, Czupryna P, Dunaj J, Swierzbinska R, Guziejko K, Rutkowski R, et al. **Evaluation of NF-kappaB concentration in patients with tick-borne encephalitis, neuroborreliosis, anaplasmosis and Anaplasma phagocythophilum with tick-borne encephalitis virus co-infection**. Cytokine 2017;90:155-60.
https://www.sciencedirect.com/science/article/pii/S1043466616305543?via%3Dihub

8. Fiorito TM, Reece R, Flanigan TP, Silverblatt FJ. **Borrelia miyamotoi Polymerase Chain Reaction Positivity on a Tick-Borne Disease Panel in an Endemic Region of Rhode Island: A Case Series**. Infectious Diseases in Clinical Practice 2017;25(5):250-4.
https://www.researchgate.net/publication/317172502_Borrelia_miyamotoi_Polymerase_Chain_Reaction_Positivity_on_a_Tick-Borne_Disease_Panel_in_an_Endemic_Region_of_Rhode_Island_A_Case_Series

9. Dedkov VG, Simonova EG, Beshlebova OV, Safonova MV, Stukolova OA, Verigina EV, et al. **The burden of tick-borne diseases in the Altai region of Russia**. Ticks Tick Borne Dis 2017;8(5):787-94.
https://www.ncbi.nlm.nih.gov/pubmed/28648773

10. Panczuk A, Tokarska-Rodak M, Koziol-Montewka M, Plewik D. **The incidence of Borrelia burgdorferi, Anaplasma phagocytophilum and Babesia microti coinfections among foresters and farmers in eastern Poland**. J Vector Borne Dis 2016;53(4):348-54.
https://www.ncbi.nlm.nih.gov/pubmed/28035112

11. Jahfari S, Hofhuis A, Fonville M, van der Giessen J, van Pelt W, Sprong H. **Molecular Detection of Tick-Borne Pathogens in Humans with Tick Bites and Erythema Migrans, in the Netherlands**. PLoS Negl Trop Dis 2016;10(10):e0005042.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5051699/

12. Krbkova L, Homola L, Hlavacova A, Mikolasek P, Bednarova J, Cermakova Z. **Assessment of antibodies against surface and outer membrane proteins of Anaplasma phagocytophilum in Lyme borreliosis and tick-borne encephalitis paediatric patients**. Epidemiol Infect 2016;144(12):2597-604.
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Other study types

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Other tick-borne co-infections

We found one diagnostic study, eight prevalence studies, and three case studies/case series on co-infections between tick-bourne diseases other than Lyme borreliosis.

Diagnostic studies

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Case studies or case series

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2.	Oxner AZ, William J. **Babesiosis in a new Englander-from primary care to intensive care**. Journal of General Internal Medicine 2012;2):S404. https://link.springer.com/article/10.1007/s11606-012-2038-0
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Comments

We performed a broad systematic literature search, trying to identify all studies mentioning diagnostic methods of tich-borne infections, regardless of study design. We may still have lost relevant studies. We limited the search to studies mentioning *tick* or *tick-bite* in title or abstract. However, not all studies on tick-bite diseases explicitly mention "ticks", and thus we performed a supplementary search without this limitation. Instead we limited the search to those described as cross-sectional studies or diagnostic accuracy studies. This gave some additional references, mainly about diagnostics of Francisella Tularensis and Babesiosis. Nonetheless, due to the study design limitation used in the supplementary search, we may have missed relevant studies.

We included case studies and case series to provide information on diagnostic methods typically used in clinical practice. Screening for inclusion of these studies was challenging, because many of the references lacked abstracts. In addition, case studies that did not use words describing *diagnosis* in title or abstracts have not been identified by the search. This may have led to some bias in the identification and inclusion of case studies and case series.

In part 1, the search for Lyme disease (borreliosis) was limited to studies on so called "chronic Lyme disease". To find as many relevant studies as possible, we also used search terms as "chronic or persistent or lingering or long-term". However, we may have lost studies that have used other descriptions for this condition.

During the reference screening we identified studies on other diagnostic methods than laboratory diagnostics. These studies did not match our inclusion criteria, but may be of relevance to the question on how to manage patients with long-term complaints after borrelia infection. See Appendix 3 for examples. This is not a comprehensive list of all relevant studies on the topic, and is not the result of a systematic literature search.

Studies in part 2 were only identified if they mentioned "co-infections" in title or abstract. There may be additional relevant studies in part 1, reporting on co-infections in the full text.

Appendix 4 presents non-systematic review articles that may refer to studies not identified in our search. For updated evidence-based recommendations about diagnostic methods of tick-borne infections, we also refer to clinical point of care tools such as NEL (Norsk elektronisk legehåndbok) https://legehandboka.no/, UpToDate

https://www.uptodate.com/contents/search and BMJ Best Practice https://bestpractice.bmj.com/.

References

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Appendix

Appendix 1: Search strategy part 1 – diagnostic tests

Part 1: Diagnostic methods

Search performed by Ingvild Kirkehei

Date of searches: 15 January 2018

The search has been peer reviewed by research librarian Elisabet Hafstad.

Search hits total: 5210 + extra search 166

Search hits after duplicate removal and removal of studies on animals: 3916

MEDLINE (Ovid)

Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Søketreff: 1828

1. exp Lyme Disease/ or Borrelia Infections/ or (borrelios* or borrelia* or lyme disease or neuroborrelios* or lyme arthritis).tw.
2. exp Chronic Diseases/ or ((chronic or post or late or persistent or lingering or long-term) adj3 (stage* or disease*)).tw. or (stage* 3 or stage* 4 or stage* three or stage* four or stage* III or stage* IV).tw.
3. ((chronic or post or late or persistent or lingering or long-term) adj5 (borrelia* or borrelios* or lyme disease*)).tw.
4. (PTLD* or CLD*).tw. and tick*.mp.
5. 1 and (2 or 3 or 4) [Kronisk borreliose]
6. Anaplasma phagocytophilum/ or (anaplasma phagocytophilum or ehrlichia phagocytophilum or cytoecetes phagocytophila or ehrlichia equi or ehrlichia phagocytophila or hge agent).tw,kw.
7. Rickettsia Infections/ or Boutonneuse Fever/ or (rickettsia helvetica or swiss agent).tw,kw.
8. Ehrlichiosis/ or (Candidatus Neoehrlichia mikurensis or Candidatus Ehrlichia walkerii).tw,kw.
9. exp Babesia/ or Babesiosis/ or (babesia* or piroplasm* or babesios*).tw,kw.
10. b* miyamotoi.tw,kw.

11. Francisella tularensis/ or Tularemia/ or (francisella tularensis or pasteurella tularensis or tularemia).tw,kw.

12. exp Bartonella Infections/ or (Bartonella or Bartonellos* or Carrion* disease or cat scratch fever* or oroya fever* or rochalimaea or verruga peruana).tw,kw.

13. or/6-12 [Andre infeksjoner]

14. exp Ticks/ or exp Tick Bites/ or exp Tick-Borne Diseases/ or (tick or ticks or Ixodes ricinus or I ricinus or Ixodes uriae* or I uriae* or ixodida* or argasida*).tw,kw.

15. 13 and 14 [Andre infeksjoner avgrenset til flåttbitt]

16. (diagnostic* or diagnosi* or validat* or reliabilit* or sensitiv* or specificity* or accuracy or gold standard* or false positiv* or false negative* or predictive value* or testing or test* performance* or xenodiagnos* or serodiagnos* or ELISA or ELISPOT or index test* or reference test* or reference standard*).tw. or (detect* or identif* or test*).ti.

17. diagnosis/ or delayed diagnosis/ or diagnosis, differential/ or exp diagnostic errors/ or "diagnostic techniques and procedures"/ or exp clinical laboratory techniques/ or "reproducibility of results"/ or "sensitivity and specificity"/ or "predictive value of tests"/

18. or/16-17 [Diagnostikk]

19. (5 or 15) and 18 [Infeksjoner OG diagnostikk]

20. (exp Lyme Disease/di or Borrelia Infections/di) and exp Chronic Diseases/

21. Anaplasma phagocytophilum/di or exp Rickettsia Infections/di or Ehrlichiosis/di or exp Babesia/di or Babesiosis/di or Francisella tularensis/di or exp Bartonella Infections/di

22. 19 or 20 or 21

23. 19 or 20 or 21 [Infeksjoner OG diagnostikk]

24. limit 23 to yr="2007 -Current"

25. (animals/ or exp Animals, Laboratory/ or exp Animal Experimentation/ or exp Models, Animal/ or exp Rodentia/) not humans/

26. 24 not 25

27. ((cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird*) not human*).ti

28. 26 not 27

29. remove duplicates from 28

30. ((or/1,6-12) and 18) or 21

31. Lyme Disease/di or Borrelia Infections/di

32. 30 or 31

33. ((systematic* adj3 review*) or meta-anal* or mapping or ((systematic* or database or literature) adj2 search*) or (review* and medline)).pt,tw.

34. 32 and 33 [Systematiske oversikter]

35. limit 34 to yr="2007 -Current"

36. remove duplicates from 35

37. 29 or 36

Embase (Ovid)

Søketreff: 2180

1. exp lyme disease/ or borrelia infection/
2. exp chronic disease/
3. 1 and 2
4. exp *lyme disease/ or *borrelia infection/ or (borrelios* or borrelia* or lyme disease or neuroborrelios* or lyme arthritis).tw.
5. exp *Chronic Disease/ or ((chronic or post or late or persistent or lingering or long-term) adj3 (stage* or disease*)).tw. or (stage* 3 or stage* 4 or stage* three or stage* four or stage* III or stage* IV).tw.
6. ((chronic or post or late or persistent or lingering or long-term) adj5 (borrelia* or borrelios* or lyme disease*)).tw.
7. (PTLD* or CLD*).tw. and tick*.mp.
8. 4 and (5 or 6 or 7) [Kronisk borreliose]
9. anaplasma phagocytophilum/ or (anaplasma phagocytophilum or ehrlichia phagocytophilum or cytoecetes phagocytophila or ehrlichia equi or ehrlichia phagocytophila or hge agent).tw.
10. Rickettsiaceae infection/ or (rickettsia helvetica or swiss agent).tw,kw.
11. exp ehrlichiosis/ or (Candidatus Neoehrlichia mikurensis or Candidatus Ehrlichia walkerii).tw.
12. exp Babesia/ or exp piroplasmosis/ or (babesia* or piroplasm* or babesios*).tw,kw.
13. b* miyamotoi.mp.
14. Francisella tularensis/ or (francisella tularensis or pasteurella tularensis).tw,kw.
15. exp bartonellosis/ or (Bartonella or Bartonellos* or Carrion* disease or cat scratch fever* or oroya fever* or rochalimaea or verruga peruana).tw,kw.
16. or/9-15
17. exp Tick/ or exp Tick Bite/ or exp Tick-Borne Disease/ or (tick or ticks or Ixodes ricinus or I ricinus or Ixodes uriae* or I uriae* or ixodida* or argasida*).tw,kw.
18. 16 and 17 [Andre infeksjoner avgrenset til flåttbitt]
19. (diagnostic* or diagnosi* or validat* or reliabilit* or sensitiv* or specificity* or accuracy or gold standard* or false positiv* or false negative* or predictive value* or testing or test* performance* or xenodiagnos* or serodiagnos* or ELISA or ELISPOT or index test* or reference test* or reference standard*).tw. or (detect* or identif* or test*).ti.
20. diagnosis/ or delayed diagnosis/ or diagnostic accuracy/ or exp diagnostic error/ or diagnostic reasoning/ or exp diagnostic test/ or diagnostic test accuracy study/ or differential diagnosis/ or exp serodiagnosis/ or exp virus diagnosis/ or xenodiagnosis/ or diagnostic procedure/ or diagnostic approach route/ or laboratory test/ or diagnostic test/ or laboratory diagnosis/ or reproducibility/ or measurement precision/ or "sensitivity and specificity"/ or predictive value/
21. or/19-20

22. 3 or 8 or 18
23. 21 and 22
24. anaplasma phagocytophilum/di or exp Rickettsiaceae infection/di or exp ehrlichiosis/di or exp Babesia/di or exp piroplasmosis/di or Francisella tularensis/di or exp bartonellosis/di
25. (Lyme disease/di or borrelia infection/di) and exp chronic disease/
26. 23 or 24 or 25
27. limit 26 to yr="2007 -Current"
28. (exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/) not (human/ or normal human/ or human cell/)
29. 27 not 28
30. ((cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird*) not human*).ti.
31. 29 not 30
32. remove duplicates from 31
33. ((systematic* adj3 review*) or meta-anal* or mapping or ((systematic* or database or literature) adj2 search*) or (review* and medline)).pt,mp.
34. exp lyme disease/ or borrelia infection/ or (borrelios* or lyme disease or neuroborrelios* or lyme arthritis).tw.
35. 34 or 16
36. (34 or 16) and 21
37. Lyme disease/di or borrelia infection/di
38. 37 or 24
39. or/36-38
40. 33 and 39
41. limit 40 to yr="2007 -Current"
42. remove duplicates from 41
43. 32 or 42

Exstra search, not limitied to “tick bites”: 166

1	anaplasma phagocytophilum/ or (anaplasma phagocytophilum or ehrlichia phagocytophilum or cytoecetes phagocytophila or ehrlichia equi or ehrlichia phagocytophila or hge agent).tw. or Rickettsiaceae infection/ or (rickettsia helvetica or swiss agent).tw,kw. or exp ehrlichiosis/ or (Candidatus Neoehrlichia mikurensis or Candidatus Ehrlichia walkerii).tw. or exp Babesia/ or exp piroplasmo-	21143

	sis/ or (babesia* or piroplasm* or babesios*).tw,kw. or b* miya-motoi.mp. or Francisella tularensis/ or (francisella tularensis or pasteurella tularensis).tw,kw. or exp bartonellosis/ or (Bartonella or Bartonellos* or Carrion* disease or cat scratch fever* or oroya fever* or rochalimaea or verruga peruana).tw,kw.	
2	(diagnostic* or diagnosi* or validat* or reliabilit* or sensitiv* or specificity* or accuracy or gold standard* or false positiv* or false negative* or predictive value* or testing or test* performance* or xenodiagnos* or serodiagnos* or ELISA or ELISPOT or index test* or reference test* or reference standard*).tw. or (detect* or iden-tif* or test*).ti.	6003398
3	diagnosis/ or delayed diagnosis/ or diagnostic accuracy/ or exp diagnostic error/ or diagnostic reasoning/ or exp diagnostic test/ or diagnostic test accuracy study/ or dif-ferential diagnosis/ or exp serodiagnosis/ or exp virus diagnosis/ or xenodiagnosis/ or diagnostic procedure/ or diagnostic approach route/ or laboratory test/ or diagnostic test/ or laboratory diagnosis/ or reproducibil-ity/ or measurement precision/ or "sensi-tivity and specificity"/ or predictive value/	2847882
4	2 or 3	7355181
5	1 and 4	8452
6	cross-sectional study/	254478
7	diagnostic accuracy/	225918
8	(cross-sectional study or (diagnostic adj3 accuracy) or diagnostic test study).tw.	206525
9	or/6-8	527290
10	5 and 9	295
11	limit 10 to yr="2007 -Current"	158
12	((chronic or post or persistent or lingering or long-term) adj5 (borrelia* or borrelios* or lyme disease*)).tw.	767
13	9 and 12	18
14	limit 13 to yr="2007 -Current"	11
15	11 or 14	166

Cochrane Library
Search hits: Cochrane Reviews 21, DARE 4, CENTRAL 102, HTA 3

#1 [mh "lyme disease"] or [mh "borrelia infections"]
#2 borrelios* or borrelia* or lyme-disease or neuroborrelios* or lyme-arthritis
#3 [mh "Anaplasma phagocytophilum"]
#4 anaplasma-phagocytophilum or ehrlichia-phagocytophilum or cytoecetes-phagocytophila or ehrlichia-equi or ehrlichia-phagocytophila or hge-agent
#5 [mh ^"Rickettsia Infections"] or [mh "Boutonneuse Fever"]
#6 rickettsia-helvetica or swiss-agent
#7 [mh ^Ehrlichiosis]
#8 Candidatus-Neoehrlichia-mikurensis or Candidatus-Ehrlichia-walkerii
#9 [mh Babesiosis] or [mh Babesia]
#10 babesia* or piroplasm* or babesios*
#11 borrelia-miyamotoi
#12 [mh ^"Francisella tularensis"]
#13 francisella-tularensis or pasteurella-tularensis
#14 [mh "Bartonella Infections"]
#15 Bartonella or Bartonellos* or Carrion* disease or cat scratch fever* or oroya fever* or rochalimaea or verruga peruana
#16 (1-#15) Publication Year from 2007 to 2018

ISI Web of Science

Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=2007-2018
Search hits: 1028

8 #6 NOT #7
7 TI=(cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or mice or mouse or "non-human" or bird* or ("in" NEAR/3 ticks) OR "in Ixodes" OR "tick host identification" or host) NOT TI=(human*)
6 #5 AND #4
5 TOPIC: (diagnostic* or diagnosi* or validat* or reliabilit* or sensitiv* or specificity* or accuracy or "gold standard*" or "false positiv*" or "false negative*" or "predictive value*" or testing or "test* performance*" or xenodiagnos* or serodiagnos* or ELISA or ELISPOT or "index test*" or "reference test*" or "reference standard*") OR TITLE: (detect* or identif* or test*)
4 #3 OR #2
3 TOPIC: ("anaplasma phagocytophilum" OR "ehrlichia phagocytophilum" OR "cytoecetes phagocytophila" OR "ehrlichia equi" OR "ehrlichia phagocytophila" OR "hge agent" OR "rickettsia helvetica" OR "swiss agent" OR "Candidatus Neoehrlichia mikurensis" OR "Candidatus Ehrlichia walkerii" OR babesia* OR piroplasm* OR babesios* OR "francisella tularensis" OR "pasteurella tularensis" OR Bartonella OR Bartonellos* OR "Carrion disease" OR "Carrion's disease" OR "cat scratch fever" OR "oroya fever" OR rochalimaea OR "verruga peruana") AND

TOPIC: (tick or ticks or "Ixodes ricinus" or "I ricinus" or "Ixodes uriae*" or "I uriae*" or ixodida* or argasida*)

2 TOPIC: ("lyme disease" OR borrelios* OR borrelia* OR neuroborrelios* OR "lyme arthritis") AND TOPIC: ((((chronic or post or late or persistent or lingering or long-term) NEAR/3 (stage* or disease*)) or ("stage* 3" or "stage* 4" or "stage* three" or "stage* four")) OR ((chronic or post or late or persistent or lingering or "long-term") NEAR/5 (borrelia* or borrelios* or "lyme disease*")))

1 TS=("lyme disease" OR borrelios* OR borrelia* OR neuroborrelios* OR "lyme arthritis" OR "anaplasma phagocytophilum" OR "ehrlichia phagocytophilum" OR "cytoecetes phagocytophila" OR "ehrlichia equi" OR "ehrlichia phagocytophila" OR "hge agent" OR "rickettsia helvetica" OR "swiss agent" OR "Candidatus Neoehrlichia mikurensis" OR "Candidatus Ehrlichia walkerii" OR babesia* OR piroplasm* OR babesios* OR "francisella tularensis" OR "pasteurella tularensis" OR Bartonella OR Bartonellos* OR "Carrion disease" OR "Carrion's disease" OR "cat scratch fever" OR "oroya fever" OR rochalimaea OR "verruga peruana") AND TS=((systematic* NEAR/3 review*) or "meta-anal*" or mapping or ((systematic* or database or literature) NEAR/2 search*) or (review* and medline))

Epistemonikos

Search hits: Systematic reviews 47, broad syntheses: 0, structured summaries: 6

Title or abstract: "lyme disease" OR borrelios* OR borrelia* OR neuroborrelios* OR "lyme arthritis" OR "anaplasma phagocytophilum" OR "ehrlichia phagocytophilum" OR "cytoecetes phagocytophila" OR "ehrlichia equi" OR "ehrlichia phagocytophila" OR "hge agent" OR "rickettsia helvetica" OR "swiss agent" OR "Candidatus Neoehrlichia mikurensis" OR "Candidatus Ehrlichia walkerii" OR babesia* OR piroplasm* OR babesios* OR "francisella tularensis" OR "pasteurella tularensis" OR Bartonella OR Bartonellos* OR "Carrion disease" OR "Carrion's disease" OR "cat scratch fever" OR "oroya fever" OR rochalimaea OR "verruga peruana" Publication year: 2007-2018

Prospero

Search hits: 2 possibly relevant

Search for Lyme, borreli*, neuroborrelios*, babesia, babesiosis, anaplasma, ehrlichia, rickettsia, swiss agent, mikurensis, piroplasm, tularensis, bartonel*, tick*

Clinical Trials.gov

Search hits: 74

Condition: Lyme disease, lyme neuroborreliosis, borreliosis, rickettsia infections, babesia OR babesiosis OR anaplasma OR ehrlichia OR rickettsia OR swiss agent OR mikurensis OR piroplasm OR tularensis OR bartonel*

ICTRP

Search hits: 65

Lyme OR neuroborreliosis OR borreliosis OR borrelia OR rickettsia OR babesia OR babesiosis OR anaplasma OR ehrlichia OR rickettsia OR swiss agent OR mikurensis OR piroplasm OR tularensis OR bartonel*

Appendix 2: Search strategy part 2 – co-infections

Search strategy Sept 3 2018

Search hits total: 1356

Search hits after duplicate removal: 853

Search hits after manual EndNote removal of animal studies: 524

MEDLINE (Ovid)

Søketreff: 334

1. exp Lyme Disease/ or Borrelia Infections/ or (borrelios* or borrelia* or lyme disease or neuroborrelios* or lyme arthritis).tw.

2. Anaplasma phagocytophilum/ or (anaplasma phagocytophilum or ehrlichia phagocytophilum or cytoecetes phagocytophila or ehrlichia equi or ehrlichia phagocytophila or hge agent).tw,kw.

3. Rickettsia Infections/ or Boutonneuse Fever/ or rickettsia*.tw.

4. Ehrlichiosis/ or (Candidatus Neoehrlichia mikurensis or Candidatus Ehrlichia walkerii).tw,kw.

5. exp Babesia/ or Babesiosis/ or (babesia* or piroplasm* or babesios*).tw,kw.

6. b* miyamotoi.tw,kw.

7. Francisella tularensis/ or Tularemia/ or (francisella tularensis or pasteurella tularensis or tularemia).tw,kw.

8. exp Bartonella Infections/ or (Bartonella or Bartonellos* or Carrion* disease or cat scratch fever* or oroya fever* or rochalimaea or verruga peruana).tw,kw.

9. Encephalitis, Tick-Borne/ or Encephalitis Viruses, Tick-Borne/ or (tick borne encephalit* or TBE).tw.

10. or/1-9

11. Coinfection/ or (co-infect* or coinfect* or superinfect*).tw,kw. or ((simultan* or co-occur* or multiple or super* or concurrent or mixed or secondary or Polymicrobial) adj infect*).tw,kw.

12. 10 and 11

13. (animals/ or exp Animals, Laboratory/ or exp Animal Experimentation/ or exp Models, Animal/ or exp Rodentia/) not humans/

14. 12 not 13

15. ((cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird* or cervid* or bovin* or equin* or in ticks) not ((cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird* or

cervid* or bovin* or equin* or in ticks) and (human* or worker* or farmer* or veterinar*))).ti.

16. 14 not 15

17. limit 16 to yr="2007 -Current"

18. remove duplicates from 17

Embase (Ovid)

Søketreff: 336

1. exp *lyme disease/ or *borrelia infection/ or (borrelios* or borrelia* or lyme disease or neuroborrelios* or lyme arthritis).tw.

2. *anaplasma phagocytophilum/ or (anaplasma phagocytophilum or ehrlichia phagocytophilum or cytoecetes phagocytophila or ehrlichia equi or ehrlichia phagocytophila or hge agent).tw.

3. *Rickettsiaceae infection/ or rickettsia*.tw.

4. exp *ehrlichiosis/ or (Candidatus Neoehrlichia mikurensis or Candidatus Ehrlichia walkerii).tw.

5. exp *Babesia/ or (babesia* or piroplasm* or babesios*).tw,kw.

6. b* miyamotoi.mp.

7. *Francisella tularensis/ or (francisella tularensis or pasteurella tularensis).tw,kw.

8. exp *bartonellosis/ or (Bartonella or Bartonellos* or Carrion* disease or cat scratch fever* or oroya fever* or rochalimaea or verruga peruana).tw,kw.

9. *tick borne encephalitis/ or (tick borne encephalit* or TBE).tw.

10. or/1-9

11. *mixed infection/ or (co-infect* or coinfect* or superinfect*).tw,kw. or ((simultan* or co-occur* or multiple or super* or concurrent or mixed or secondary or Polymicrobial) adj infect*).tw,kw.

12. 10 and 11

13. (exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/) not (human/ or normal human/ or human cell/)

14. 12 not 13

15. ((cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird* or cervid* or bovin* or equin* or in ticks) not ((cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird* or cervid* or bovin* or equin* or in ticks) and (human* or worker* or farmer* or veterinar*))).ti.

16. 14 not 15

17. limit 16 to yr="2007 -Current"

18. remove duplicates from 17

ISI Web of Science

Søketreff: 678

#1 not #2
3 Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI
Timespan=2007-2018
# TI=(((cattle or deer or livestock or dog or dogs or cat or cats
2 or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird* or cervid* or bovin* or equin* or "in ticks") not ((cattle or deer or livestock or dog or dogs or cat or cats or animal* or rodent* or farms or farm or canine or wild game or mouse or mice or horse* or mammal* or rabbit* or bird* or cervid* or bovin* or equin* or "in ticks") and (human* or worker* or farmer* or veterinar*))))
Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI
Timespan=All years
# **TOPIC:** ("lyme disease" OR borrelios* OR borrelia* OR
1 neuroborrelios* OR "lyme arthritis" OR "anaplasma phagocytophilum" OR "ehrlichia phagocytophilum" OR "cytoecetes phagocytophila" OR "ehrlichia equi" OR "ehrlichia phagocytophila" OR "hge agent" OR "rickettsia*" OR "swiss agent" OR "Neoehrlich*" OR "Ehrlichia walkerii" OR babesia* OR piroplasm* OR babesios* OR "francisella tularensis" OR "pasteurella tularensis" OR tularemia OR Bartonella OR Bartonellos* OR "Carrion disease" OR "Carrion's disease" OR "cat scratch fever" OR "oroya fever" OR rochalimaea OR "verruga peruana" or TBE or tick borne encephalit*) *AND* **TOPIC:** (co-infect* or coinfect* or superinfect* or ((simultan* or co-occur* or multiple or super* or concurrent or mixed or secondary or Polymicrobial) NEAR/1 infect*))
Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI
Timespan=All years

EPISTEMONIKOS

Search hits: 8

(title:(("lyme disease" OR borrelios* OR borrelia* OR neuroborrelios* OR "lyme arthritis" OR "anaplasma phagocytophilum" OR "ehrlichia phagocytophilum" OR "cytoecetes phagocytophila" OR "ehrlichia equi" OR "ehrlichia phagocytophila" OR "hge agent" OR "rickettsia*" OR "swiss agent" OR "Neoehrlich*" OR "Ehrlichia walkerii" OR babesia* OR piroplasm* OR babesios* OR "francisella tularensis" OR "pasteurella tularensis" OR tularemia OR Bartonella OR Bartonellos* OR "Carrion disease" OR "Carrion's disease" OR "cat scratch fever" OR "oroya fever" OR rochalimaea OR "verruga peruana" OR TBE OR tick borne encephalit*)) OR abstract:(("lyme disease" OR borrelios* OR borrelia* OR neuroborrelios* OR "lyme arthritis" OR "anaplasma phagocytophilum" OR "ehrlichia phagocytophilum" OR "cytoecetes phagocytophila" OR "ehrlichia equi" OR "ehrlichia phagocytophila" OR "hge agent" OR "rickettsia*" OR "swiss agent" OR "Neoehrlich*" OR "Ehrlichia walkerii" OR babesia* OR piroplasm* OR babesios* OR "francisella tularen-

sis" OR "pasteurella tularensis" OR tularemia OR Bartonella OR Bartonellos* OR "Carrion disease" OR "Carrion's disease" OR "cat scratch fever" OR "oroya fever" OR rochalimaea OR "verruga peruana" OR TBE OR tick borne encephalit*))) AND (title:(co-infect* OR coinfect* OR superinfect* OR ((simultan* OR co-occur* OR multiple OR super* OR concurrent OR mixed OR secondary OR Polymicrobial) AND infect*)) OR abstract:(co-infect* OR coinfect* OR superinfect* OR ((simultan* OR co-occur* OR multiple OR super* OR concurrent OR mixed OR secondary OR Polymicrobial) AND infect*)))

Appendix 3: A selection of studies on diagnostic methods other than laboratory diagnostics

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Appendix 4: Review articles

Multiple infections

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